MIT'S MAGAZINE OF INNOVATION

TECHNOLOGY REVIEW

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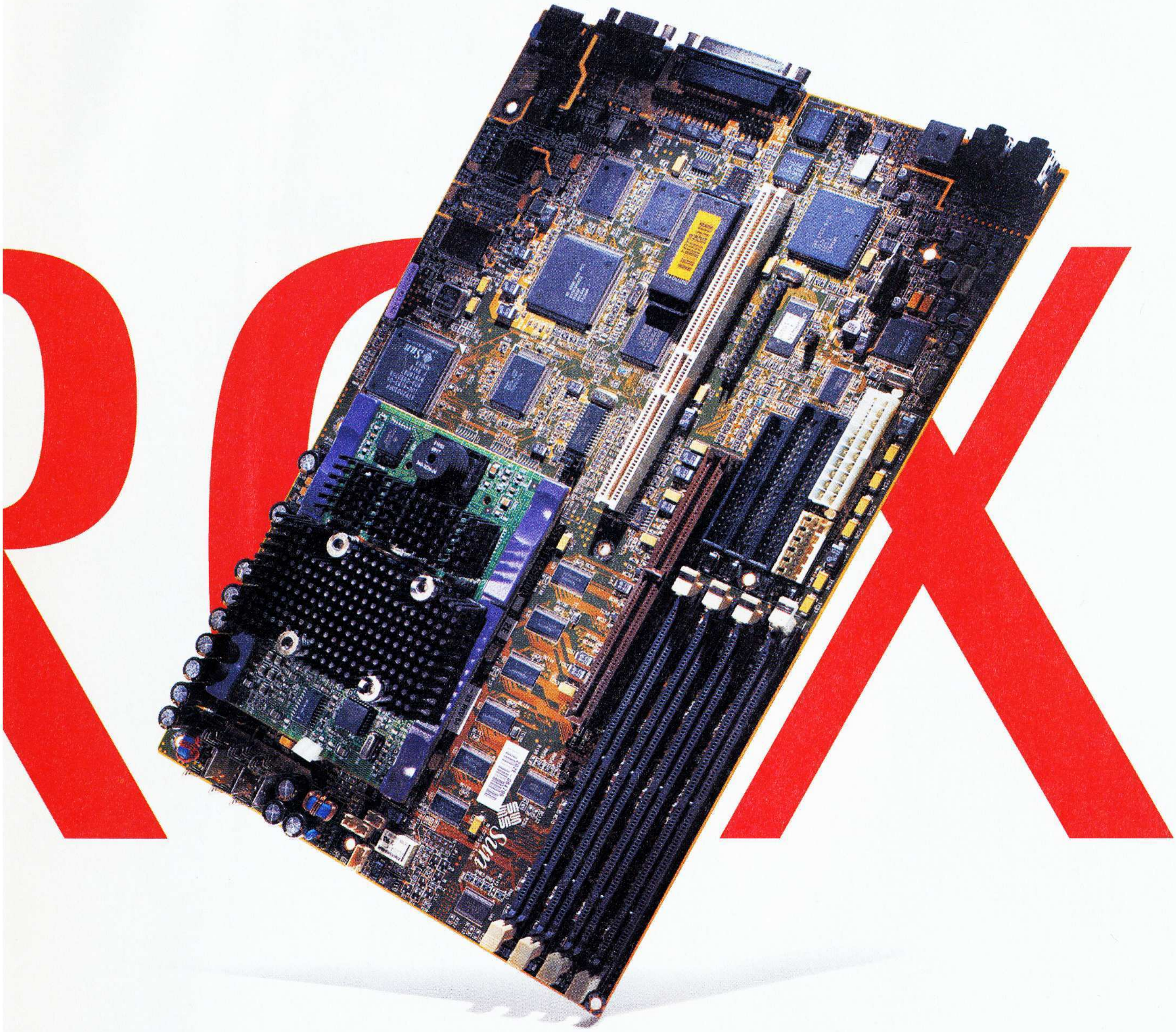

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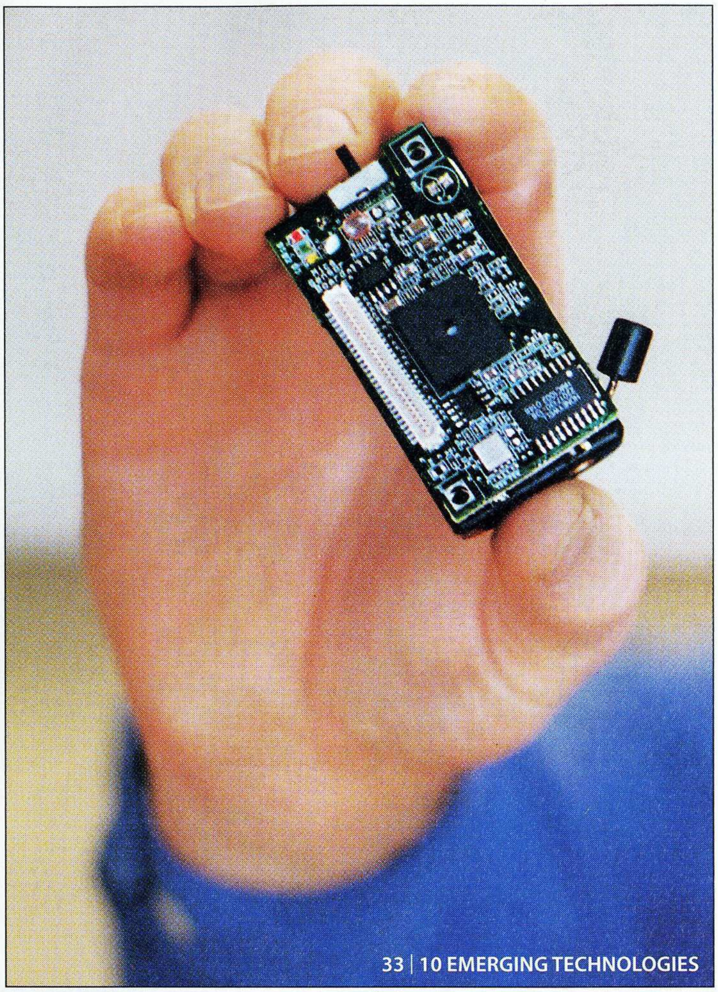

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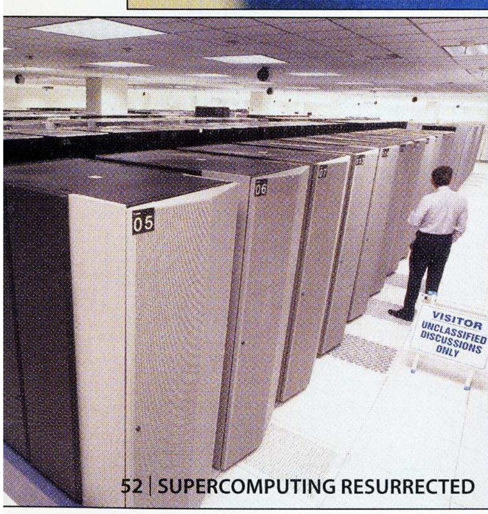

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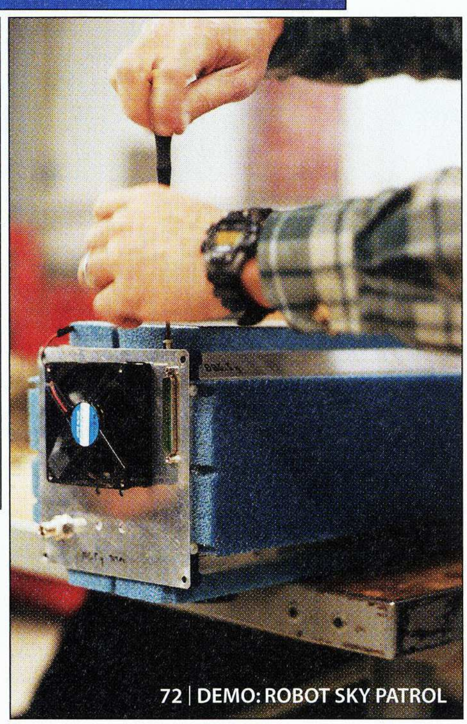

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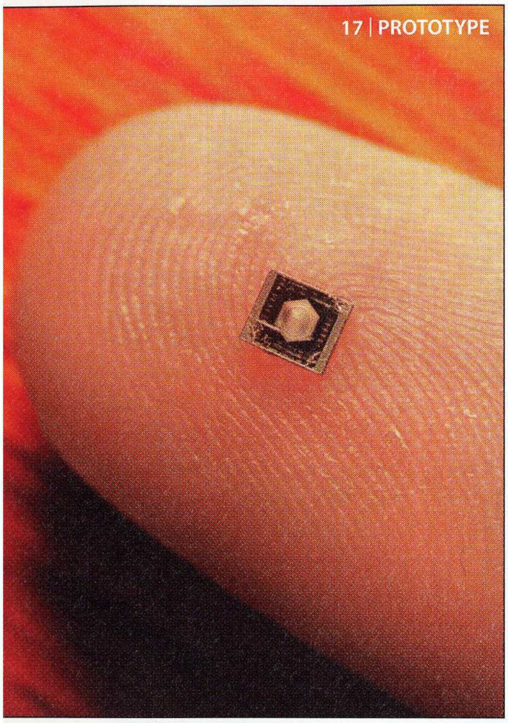

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TO CONGRESS: LET'S GET PHYSICAL

The United States is waging a campaign it cannot afford to lose: the effort to nurture the basic, often long-shot research that drives much economic growth. Understanding this, the nation has for years led the world in research-and-development investment. But it takes due diligence to stay atop the effort. The good news is that federal funding for life sciences research has soared in the past decade. But the largesse has been unevenly distributed. Uncle Sam has not been investing enough—or particularly wisely—in the fundamental physical sciences, mathematics, and engineering research necessary to ensure new computing architectures, alternative energy sources, improved forms of transportation, and other underpinnings of a vibrant economy.

Redressing this imbalance must be a first order of business for the new Congress. The previous Congress left Washington, DC, having appropriated funds for nothing but the Defense Department for fiscal year 2003, which began last October 1. This means that the modest plans afoot to bolster the physical sciences—chiefly in the budget of the National Science Foundation—are still on shaky ground. Its appropriation must be finalized. Even more critical is the fiscal 2004 budget due to be taken up this month. Failure to significantly boost spending on physical sciences and engineering—not just at NSF, but also at the Department of Energy, NASA, and fellow agencies—would be a grave mistake.

For several years, leaders in business, government, and academia have pressed for this change. An important 2001 National Research Council report, *Trends in Federal Support of Research and Graduate Education*, noted that from 1993 to 1999, the portion of the federal R&D portfolio devoted to physical sciences and engineering slipped from 37 percent to 31 percent. Moreover, funding for each of five critical fields—physics, geological sciences, and mechanical, chemical, and electrical engineering—declined a worrisome 20 percent or more. Things haven't changed much since.

I could cite the Cold War's end and other conditions that contributed to this crisis. But let me try another tack. Read our special report, "10 Emerging Technologies That Will Change the World" *(p. 33)*. Then ask yourself, What will a report like this look like 10 years from now if the government continues to neglect investment in these critical areas?

Or turn to "Supercomputing Resurrected" *(p. 52)*. This powerful story showcases how Japan, with its Earth Simulator, has taken the lead in supercomputing—and how U.S. neglect of this vitally important technology has left the nation scrambling to catch up. Indeed, Japan's success points to a golden age of big scientific computing that promises payoffs in global-climate modeling, understanding how the body's proteins work, and simulations of similarly complex systems. The United States initially responded to the $350 million Japanese effort with a few $3 million research grants to pursue new supercomputing architectures. Last November the Energy Department upped the ante by awarding a $267 million contract to IBM to build a faster supercomputer than the Earth Simulator. These may be prudent first steps. But without a commitment that goes beyond playing catch-up, the nation risks falling further behind and delaying important discoveries. Yes, I realize that this sounds like the same argument we heard about Asia and Europe in the 1980s. But vigilance must be eternal.

From 1993 to 1999, federal funding in each of five critical fields—physics, geological sciences, and mechanical, chemical, and electrical engineering—declined a worrisome 20 percent or more.

The Bush administration's response to the need to increase funding for the physical sciences has been lukewarm. Last fall the President's Council of Advisors on Science and Technology issued a draft letter echoing many of these concerns. However, the letter was never finalized and seems to have had no influence on budget priorities. I worry that the new Congress, taking its cue from the White House, will be more interested in cutting taxes than investing in fundamental research. Of course, national security is a big issue: war with Iraq looms, and the specter of terrorism darkens everything. So maybe the folks in Washington will keep in mind that a balanced investment in science and technology is also a matter of national security.

It's time to get physical. *—Robert Buderi*

GET THE POINT—THE POINT OF IMPACT

This issue marks the debut of a new department, Point of Impact *(p. 78)*. Our goal is to present, in an accessible and engaging way, leading thinkers' ideas about the impact of technology on society, business, and people's lives. In each issue, we will present a one- or two-page interview with a researcher, business executive, government official, or other insightful and opinionated observer on topics causing a stir in technology circles. First up: biophysicist and ethicist Gregory Stock on what he says is the inevitability of parents' designing their children's genetic composition.

As we add the new department, we close an old one, Upstream, in which we spotlighted promising technologies whose payoffs likely lie farther off than those covered in our other pages. We will continue to cover Upstream-like ideas in our Innovation section.

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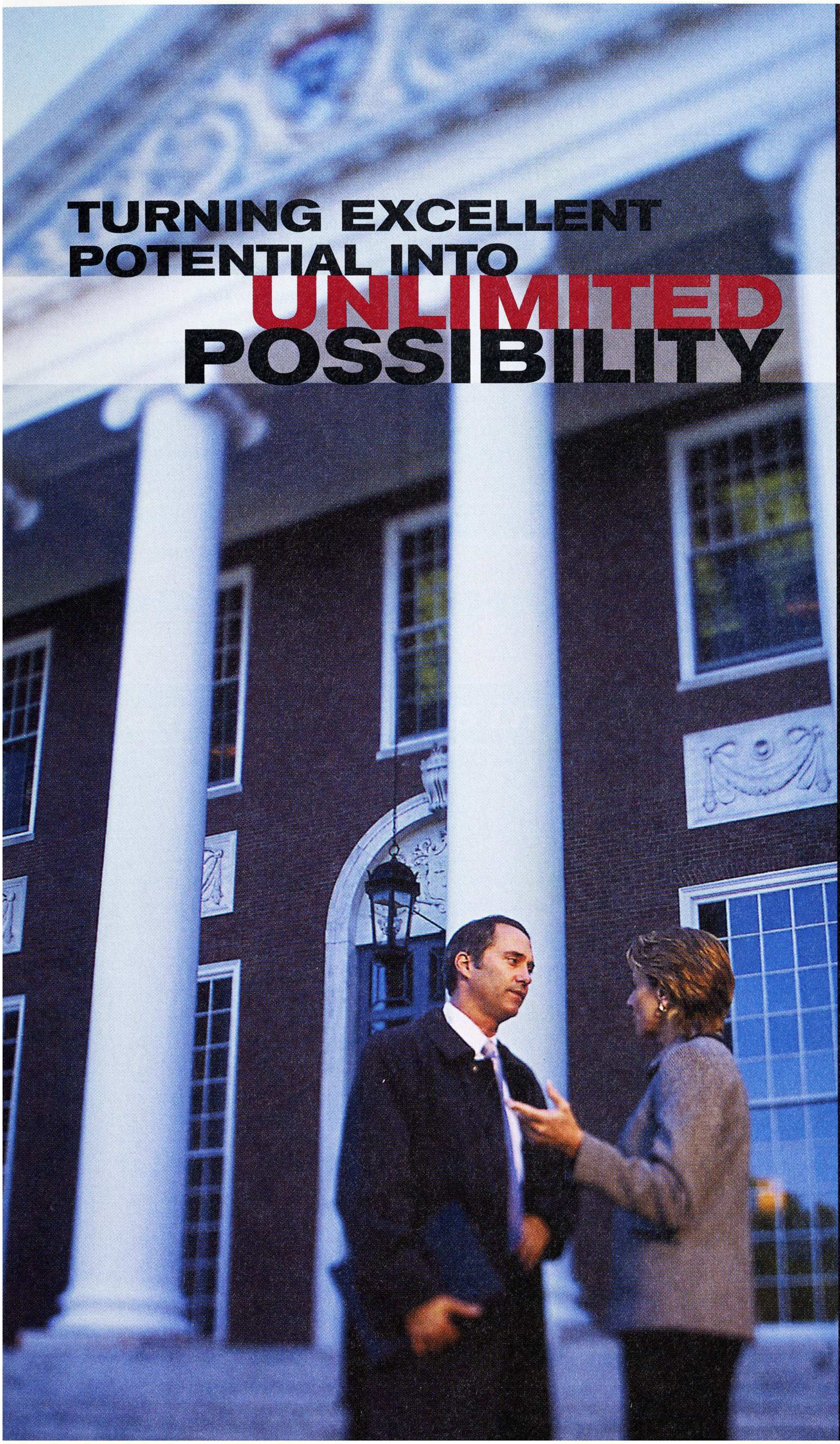
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VICE PRESIDENT AND GENERAL MANAGER
Martha Connors, martha.connors@technologyreview.com

VICE PRESIDENT, SALES AND MARKETING
Kate Dobson, kate.dobson@technologyreview.com

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J. R. "Matt" Mattox
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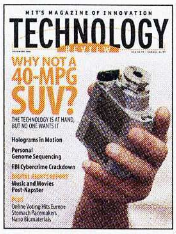
WHY NOT A 40-MPG SUV?

After overcoming my initial shock from reading Mark Fischetti's "Why Not a 40-mpg SUV?" (*TR* November 2002), I realized that this article reaffirmed my beliefs about the motivations and roles of new technology, business, and government. I applaud Fischetti for rightly pointing out that the auto industry has little motivation to change without a mandate from Washington or an outcry from the public. Only then will new technologies serving noneconomic needs be implemented. The answer to the question "Why Not a 40-mpg SUV?" will be found with the politicians and, ultimately, the voters.

D. Fred Ackerman
Richmond, CA

We're not going to see 40-mpg SUVs anytime soon, and that's not because Detroit is incompetent. Bigger and heavier SUVs outsell smaller and lighter vehicles for a simple reason: U.S. drivers want them. Actually, so do drivers elsewhere. Mercedes doesn't make its largest cars for the U.S. market alone; plenty of Germans love big and fast vehicles, too. America's crime is not to love excess—it's to afford it.

Rick Blake
Biddeford, ME



We're not going to see 40-mpg SUVs anytime soon, and that's not because Detroit is incompetent. SUVs outsell lighter vehicles for a simple reason: U.S. drivers want them.

Ford is coming out with its Escape model, a hybrid gasoline-electric SUV, in 2003; some of us have been waiting two years for it. Toyota and Volkswagen say they will be selling hybrid SUVs within five years. The technology is now being brought to production. Your article didn't mention the possibility that car manufacturers might finally be listening now that we are worried about our oil consumption. I don't work for a car company. I'm just a consumer patiently waiting for a car that does its part for the environment, as well as for my pocketbook.

Tracy Greeley-Adams
Cincinnati, OH

Almost every purported solution reported in your article is so far from existing technology that it makes the development of flying cars seem easy by comparison. Continuously variable transmissions, for instance, haven't proved they can stand up to the high torque requirements of a heavy-duty fleet truck. Direct injection still has

serious noise problems that stem from low-idle detonation. In the future, it would be nice to read articles that discuss the ways technology is helping overcome these obstacles, rather than an attack on the automotive industry.

Ed Twiss
Fort Worth, TX

POST-NAPSTER: MOVIES

In response to your report, "Digital Entertainment Post-Napster: Movies," (*TR* November 2002): Even though some people download movies, I never fail to see queues at cinemas during weekends. Nothing can beat the experience of seeing an action hero on the big screen. When the VCR was invented, Hollywood prophesied that the so-called piracies made possible by these machines would bring about the demise of cinema. That didn't happen. Hollywood should stop wasting resources and find new means to derive revenues from its creative output.

Lim Yung Hui
Kuala Lumpur, Malaysia

POST-NAPSTER: MUSIC

David Kushner's article on copy-protected audio CDs did a great job of explaining the technical and legal issues surrounding this important consumer issue. If the music industry goes through with its plans to sell only copy-protected CDs, my family will have to stop buying new CDs. The problem is that copy-protected CDs won't play on our home theater system, DVD player, or two MP3 players. To protect substantial investments in home entertainment systems, I expect to see legal challenges by consumers to the switchover to copy-protected CDs.

Richard M. Smith
Brookline, MA

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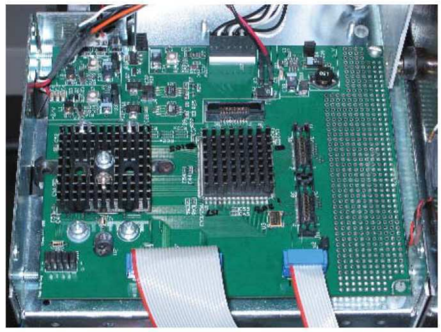
CYBERCRIME

Simson Garfinkel's article "The FBI's Cybercrime Crackdown" (*TR* November 2002) was very interesting, but I was shocked at the laxity of sentences imposed on convicted hackers. The individuals listed in the "Hall of Cyberinfamy" are some of the most malicious and destructive hackers in history, but none served more than a few years in prison. It's bad enough that so few hackers are ever caught and convicted, but these sentences are a joke. If law enforcement is to serve as a deterrent, criminals must believe that there is a chance of being caught and that severe punishment will follow. In the case of cybercrime, we appear to be failing on both counts.

Bill Jonsson
Charleston, SC

CINEMATIC COUNTERMEASURE



An electronic system foils movie pirates.

The expansion of digital cinema could be a boon for movie pirates who use camcorders to record films from theater screens and then sell the copies on the streets of New York City and Bangkok. But Cinea, a startup in Herndon, VA, is working with Princeton, NJ-based Sarnoff to develop technology that will make such recordings worthless. Recordings of conventionally projected films contain pulses of black because camcorders catch the brief moments during which the projector light flicks off and the next frame scrolls into place. A digital projector, however, emits continuous streams of light, allowing a pirate to record a great image. Through specially designed software and hardware, researchers at Cinea can control the microscopic mirrors that reflect each pixel of light toward the projector's lens. Turning the mirrors back and forth in a pattern creates milliseconds-long distortions in the image. Theatergoers don't see them, but camcorders pick up the distortions in the same way they record the flickers of conventional projection, says Cinea CEO Robert Schumann. Cinea has demonstrated its process using still images, and with a $2 million grant from the federal government's Advanced Technology Program, the company plans to have a system ready for testing at a large-screen movie theater within two years.

Focusing on just part of an image speeds downloads.

IN FOCUS

Stare a moment at this *O*. Chances are you can't make out the words at either end of this line. That's because extreme detail can be resolved only by the small slice of the human retina called the fovea. Our eyes compensate for this limitation by jumping from spot to spot. Now researchers are mimicking this phenomenon in an effort to avoid sending "wasted" pixels in digital images over the Internet.

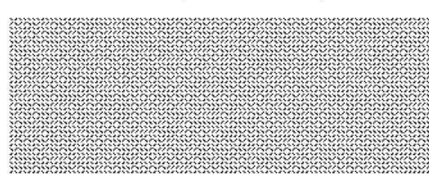
Foveal Point, server-based software developed by New York University computer scientist Chee Yap, sends high-resolution detail only for the area of an image at which a user's mouse is pointing. The user specifies that area's radius, and the surrounding image remains indistinct. The result: the bandwidth needed to download images such as satellite photos can be cut by as much as 95 percent, depending on the size of the foveated area and the haziness of the background. Yap hopes to license the software to a company that will adapt it for commercial Web browsers and mobile devices. "Every browser should have such 'smart' viewers," Yap says, so that users can "go to any site and view arbitrarily large and high-resolution images."

TREATMENT TRANSPORTER

The molecular system that shepherds antibodies from a mother's milk to her baby's bloodstream may soon provide a painless alternative to drug injections. Molecules in the lining of a baby's digestive tract pull antibodies from milk before they're digested and escort them to the blood. This mechanism also operates in the upper-lung and nasal passages, and it remains active throughout life. Syntonix Pharmaceuticals of Waltham, MA, plans to exploit the pathway by fusing antibodies to drug molecules that are conventionally delivered by injection. Entering the body via an inhaler, nasal spray, or a pill, the fused drug molecule takes the antibody shortcut to the bloodstream, says Alan Bitonti, the company's vice president for research. Last year, Syntonix began a human trial of a fused version of the red-blood-cell booster erythropoietin; several other fused drugs are in preclinical testing.

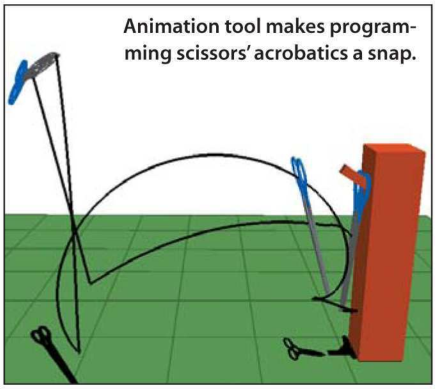
DOCUMENT FIXER

Coffee spill obliterate part of that important letter? All you need is a paper towel and some document-embedding technology from Palo Alto Research Center in Palo Alto, CA. Then you can clean up the mess and reconstruct the full page—words and images alike—in seconds. The technology, which PARC is seeking to license, starts by encoding the original document in a series of slashes—each just one-half millimeter across—that represent ones and zeroes. These "glyphs" may be printed as an unobtrusive gray screen on the back of the original. Scanning any 75 percent of a document's gray screen gives a computer all the information it needs to rebuild the original. The key to this process is image compression technology that can render images with a minimum of glyphs, as well as redundancy within the glyphs and error correction software that fills in missing data. "Just as the Internet can recover from packet loss; we can recover from page loss," says Jeff Breidenbach, the system's developer.



Glyphs encode this story's first three sentences.

IMAGE CREATED USING PARC'S GLYPHSERVER (DOCUMENT); COURTESY OF CHEE YAP AND TING-JEN YEN (IN FOCUS); COURTESY OF CINEA (CINEMATIC)



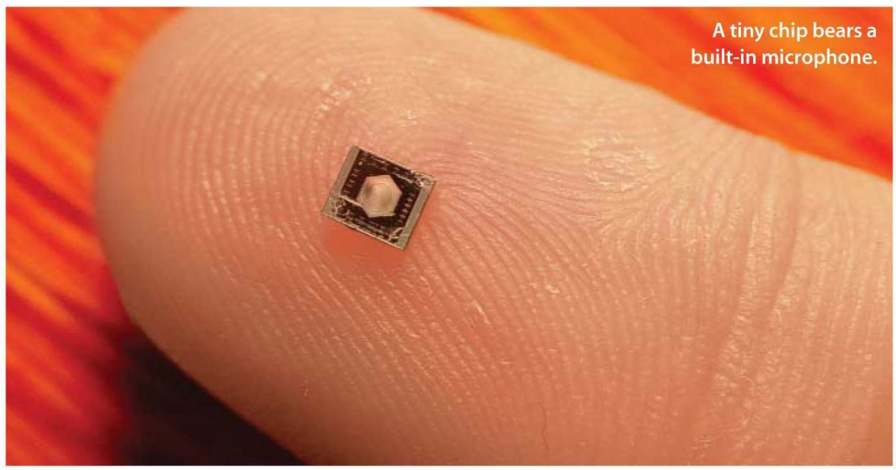
Animation tool makes programming scissors' acrobatics a snap.

POINT-AND-CLICK ANIMATION

Software based on physical models helps artists create realistically animated graphics, but getting an on-screen object to wind up in a particular place is a tedious trial-and-error process. Enter Jovan Popovic of MIT's Laboratory for Computer Science. He has developed software that gives animators interactive, real-time control over animated graphics. To make a pair of scissors bounce off the floor and land on a coatrack, say, the animator simply clicks on the scissors and drags them first to the floor and then to the rack, determining the scissors' path on the screen. The computer calculates the starting conditions needed to make the journey happen and does the math that generates realistic animation. Popovic, who did the research while he was a student at Carnegie Mellon University, says his tool will make movie and video game sequences—such as rolling dice, bouncing balls, and colliding objects—more believable. He has begun negotiations to license the software.

IMPRESSIVE CHIPS

By helping to identify the proteins involved in fundamental cellular reactions, protein chips could become powerful aids in disease diagnosis. Aspira Biosystems, a startup in South San Francisco, CA, has developed a way to make protein chips that are more reliable and can detect more proteins than existing chips. Most of today's protein chips rely on nanoscopic spots of special proteins to interact with and capture other proteins. Because the molecules are so finicky, however, chips are available for only a few types of proteins. Aspira's system lets researchers make casts of short fragments of proteins in a polymer; these casts, arrayed on a chip, can selectively capture the matching proteins from a mixture of molecules. Using this technique, it should be possible to make chips that can latch onto virtually any protein, making way for the diagnostic tests that are needed to make personalized medicine a reality. Next year Aspira plans to begin selling the chips to pharmaceutical and biotechnology companies for use in drug discovery; diagnostic applications will follow.



A tiny chip bears a built-in microphone.

ONE-CHIP AUDIO

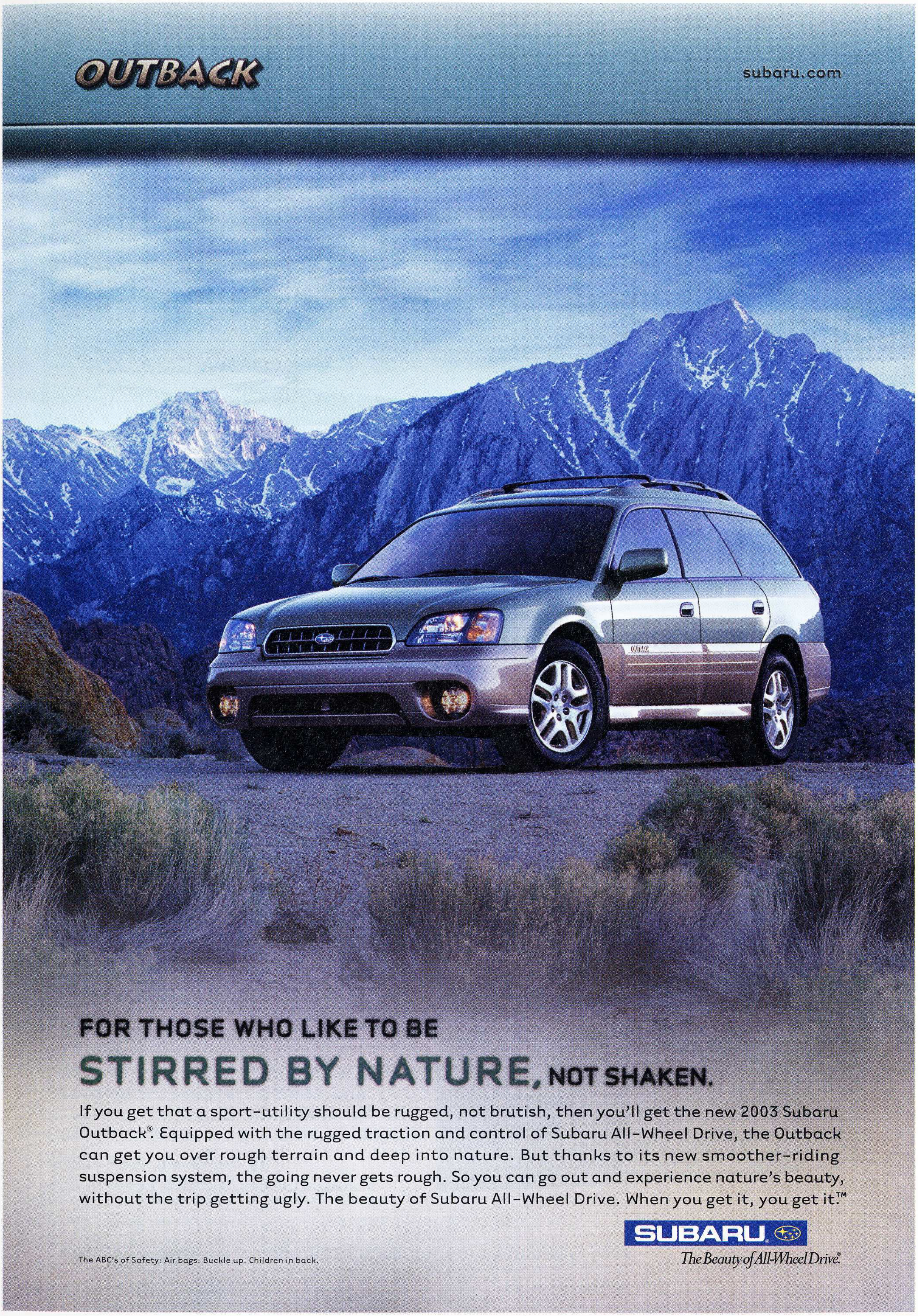
In the race to make cell phones and other audio devices smaller and cheaper, one company has found a way to put the sensing and processing onto a single chip. Akustica, a Pittsburgh spinoff from Carnegie Mellon University, has built multiple microphones onto a chip by etching meshes of tiny beams over cavities in its surface and applying a polymer coating that vibrates. Unlike competing systems that require separate assemblies for processors and acoustic parts, each of these chips is fabricated in one piece using standard automated techniques. The chips are, therefore, durable, reliable, and cheap to mass-produce. Akustica has put as many as 64 microphones onto a two-by-two-millimeter signal processor about the size of a sesame seed. Considerably smaller than what's inside today's cell phones and hearing aids, the chip, says CEO Jim Rock, can tell where sounds are coming from and can reduce background noise for a fraction of conventional manufacturing costs. Akustica plans to begin volume production within two years.

BATTERY MANAGER

Throw those jumper cables away. A sensor-and-software system under development at Stuttgart, Germany-based Bosch promises an end to weak or dead batteries, which account for one in seven car breakdowns. The unit, housed in a box the size of a deck of cards, monitors the battery's ability to hold its charge and partially regulates power flows throughout the car. If the battery charge falls below a threshold level, for example, the system might raise the engine idle rate briefly to speed recharging or cut off power to low-priority systems such as heated seats, says Günter Threin, an electrical engineer at Bosch who codeveloped the system. Using proprietary software that models the way batteries deteriorate with age, the system can warn a driver to replace the car battery well before the starter motor starts to struggle. An early version of the technology will be installed in some luxury car models this year; improved and lower-cost versions for wider applications are expected by 2005.

Sensors and software keep car batteries in shape.

COURTESY OF BOSCH (BATTERY); COURTESY OF AKUSTICA (ONE-CHIP); COURTESY OF JOVAN POPOVIC (POINT-AND-CLICK)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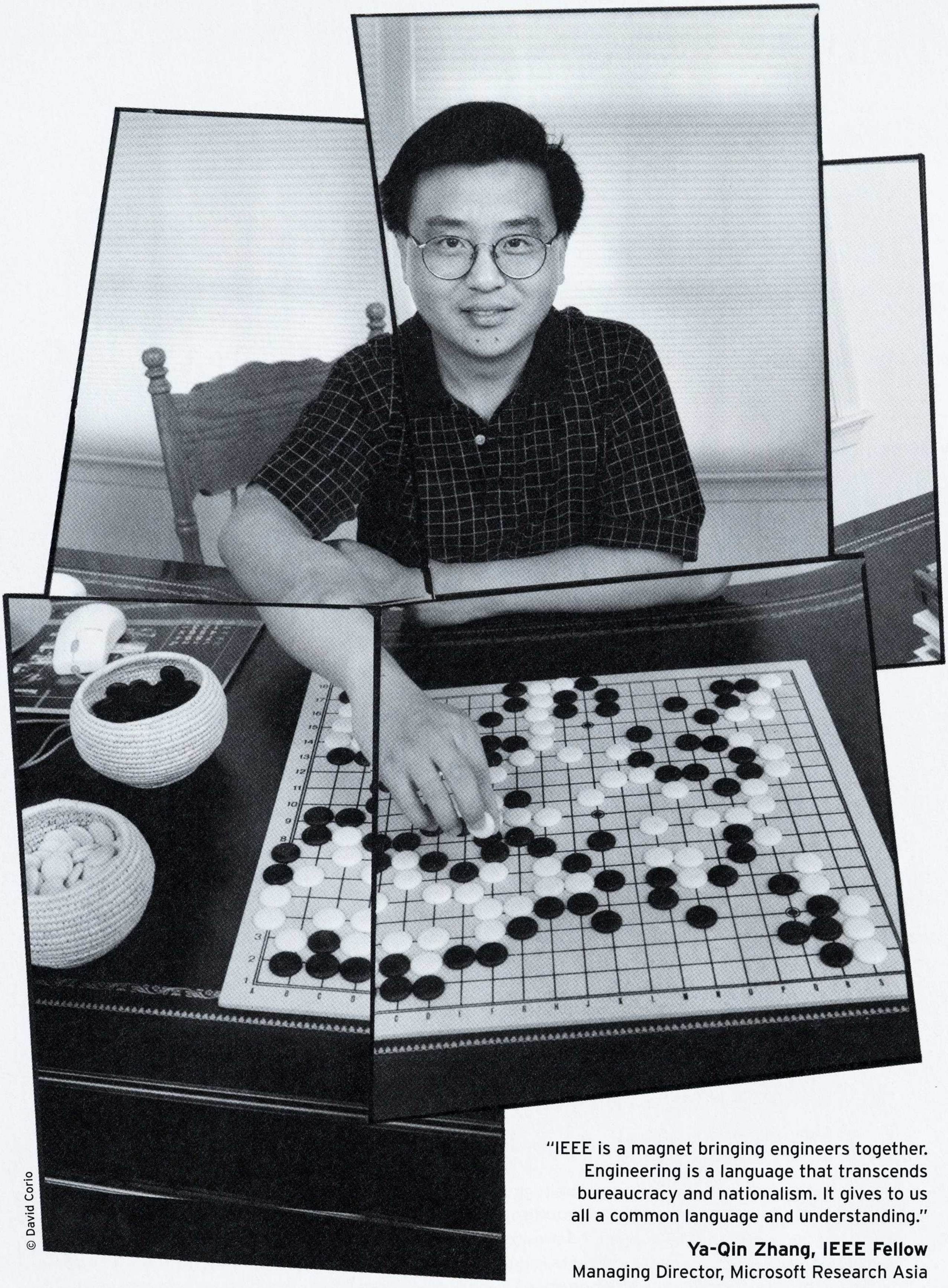

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Ya-Qin Zhang, IEEE Fellow

Managing Director, Microsoft Research Asia

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THE WEIGHT OF INNOVATION

If you're an adult U.S. citizen, chances are you're overweight. Indeed, there is almost a one-in-five chance that your body-mass index is greater than 30, which technically qualifies you as obese. Yet somehow, surveys say that at any given moment, almost 40 percent of the country's population is attempting a diet. *Bon appétit*!

The lipid-losing marketplace is growing even faster than the population's waistline. Weight loss is conservatively a $30 billion a year industry in the United States. Consequently, few industries are more competitive, more profitable, or more innovative. Can't summon the willpower to sustain a diet? Pop an appetite suppressant. Lack the patience to shed those unsightly pounds slowly? Consider liposuction. Still morbidly obese after failing diet after diet? A stomach reduction or stapling may be the surgical solution for you. The caloric continuum stretches from Diet Coke to nascent genomic techniques for reengineering the digestive tract.

What makes the weight loss enterprise so intriguing is just how cleverly it gets people to reframe the fundamental questions asked by anyone giving serious consideration to adopting an innovation. The most important question always asked, of course, is "Does it work?" But the question that will ultimately make or break the adoption is "Is it worth it?"

As any dieter or candidate for elective surgery knows, that question concerns issues of self-image and safety as much as personal finance. The ability to perform liposuction under local rather than general anesthesia has contributed enormously to the procedure's popularity. Medical reports that link many diet pills to irreversible organ damage, on the other hand, have reduced the appeal of such remedies.

Weight Watchers International offers a superb case study that demonstrates the way a seemingly trivial innovation utterly transformed how the company's clients asked themselves "Is it worth it?" The company radically simplified the dieter's food selection process by assigning each food item a point value and eliminating the need to tally calories.

Most vegetables have no points per serving; most pieces of fruit are worth one point; a Big Mac rates a whopping 14 points. A typical dieter might be instructed to consume from 22 to 27 points' worth of food each day and might be allowed to "bank" the unused points from one day to the next depending upon weekly intake.

This simple reframing sent the company's compliance and satisfaction rates soaring. Survey after customer survey confirmed that dieters found counting points to be far easier and less judgmental than counting calories and selecting the "right" foods. (Indeed, some users objected that the point system might be *too* flexible.)

The point-counting weight-loss system, which began in the United Kingdom in the mid-1990s, was so successful that it was swiftly exported to the United States. The innovation had legs. The executive responsible became Weight Watchers' CEO. The company, which went public in the teeth of the IPO recession in 2001, has seen both its market share and its stock price rise. And the point system, which the company has patented of course, is credited with transforming the Weight Watchers' lifestyle vocabulary.

Weight Watchers still relies heavily on support group meetings, where attendees affirm and reinforce their lifestyle changes. But changing the value vocabulary from "calories" and "food groups" to "points" has changed the conversations. Group members now have a common language that lets them talk more comfortably about their own eating habits as well as others', says a Weight Watchers spokeswoman.

But the firm also has little hesitation using other tactics to make it easier for clients to answer "Is it worth it?" Weight Watchers played a critical role in the recent decision of the U.S. Internal Revenue Service to make doctor-prescribed weight-loss programs tax-deductible. The tax code now subsidizes the Weight Watchers innovation. By contrast, fat-free foods and cosmetic surgeries are not tax-deductible.

What makes the weight loss enterprise so intriguing is just how cleverly it gets people to reframe the fundamental question asked by anyone adopting an innovation: "Is it worth it?"

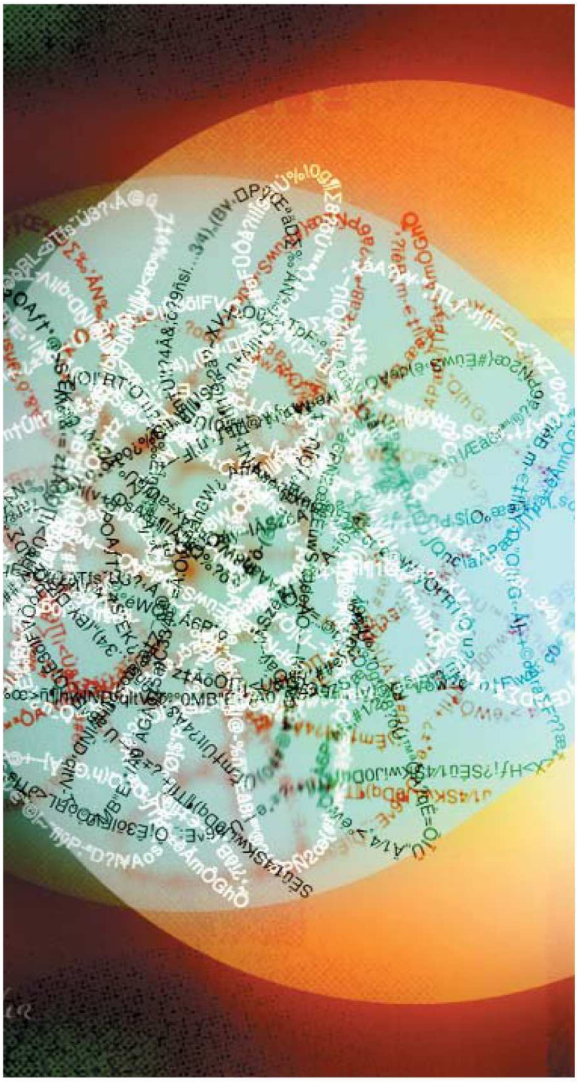
Continuous competition in this marketplace imposes "Is it worth it?" tests for the unhappily overweight. Suppose a new generation of genomics or fat-blocking chemicals inspires a new kind of patch or pill. What if liposuction becomes even less expensive and invasive than it is now? What happens if the IRS provides such treatments with the same kind of tax breaks it now gives weight reduction programs? Altering the trade-off between the discipline of tallying points and the ease of popping pills, such public policy shifts could force dieters to revisit their core innovation-adoption question.

"You have to understand," says the Weight Watchers spokeswoman, "that pills and surgery only deal with the symptoms, not the problem itself." That focus might turn out to be its ultimate weakness. Often the most profitable innovations are the result of treating symptoms and not the causes: consider the success of the antidepressant Zoloft.

The challenge of such approaches is what makes tomorrow's market for weight reduction innovation so interesting. Will the diet innovators make more from treating the symptoms of superfluous avoirdupois or from attacking its cause? Let's weight and see. TR

HANDING OVER THE KEYS

Security chips are on the way, but are they trustworthy?



In the computing industry's decades-old arms race against hackers and pirates, the bad guys continually find and exploit holes in security software, and the good guys rush in to patch them. Now for the first time, companies are rolling out a hardware-based security technology that promises to change the fundamental architecture of the personal computer. Whether the security technology threatens users' control over their own software and data, however, remains a hotly contested concern.

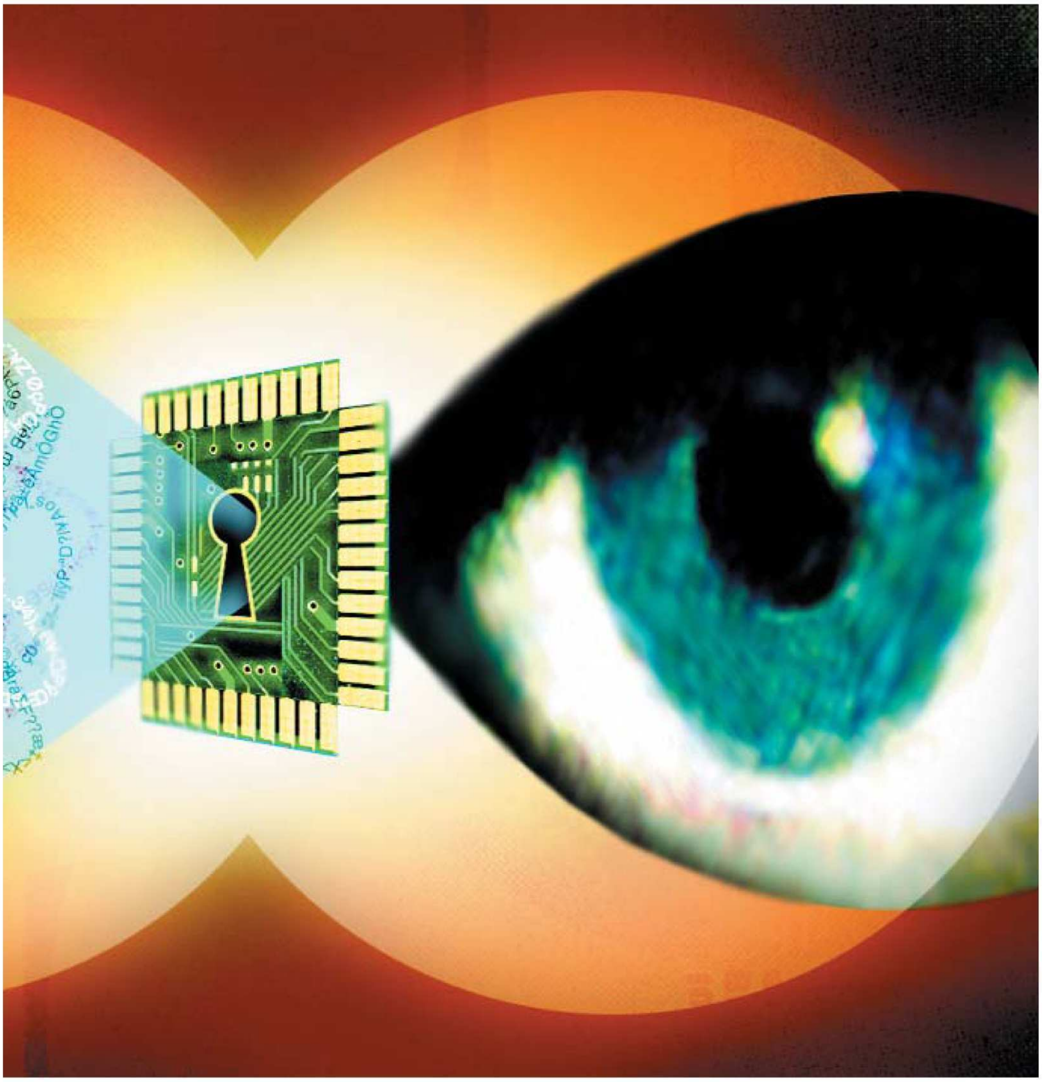
An industry consortium that includes IBM, Intel, Hewlett-Packard, and Microsoft has created specifications for a new microchip that—independent of a computer's main processor—would store special keys for encrypting and decrypting data. Keys stored on a separate chip are beyond the reach of hacker software, so they can keep encrypted data secure. "It's like having a little safe inside your PC," says Bob Meinschein, an engineering manager at Intel Research and member of the technical committee of the companies' Trusted Computing Platform Alliance, formed in 1999.

Since last June, IBM has been selling computers that incorporate the chips, and the company expects that the chips will eventually be in smaller computing devices such as personal digital assistants and cell phones. Microsoft has gone a step further and is developing a related but independent approach dubbed Palladium. That technology incorporates both Microsoft's own designs for special hardware and a new "nexus," a trusted suboperating system that will run programs configured to take advantage of the hardware. It will be included in future versions of the company's Windows operating system.

The heart of both schemes is a special microchip, a tiny Fort Knox for secret data, that includes mathematical keys to encrypt and decrypt information so that no one but the machine's authorized user can read it. (Computers today routinely handle such encryption when they send credit card information over the Web, but most computers store keys on their hard drives, which are highly vulnerable to hackers.) And this chip doesn't simply store secrets; it also takes over basic cryptographic operations, so software configured to take advantage of the chip's capabilities can ask the chip to encrypt data on its computer's hard drive. Because each chip would come with unique encryption keys, encrypted information would be accessible only to the program and the computer that originally sealed it.

To keep hackers from commandeering machines remotely, both plans include features that allow data access only to a user who is physically present. Palladium, for instance, checks whether commands are really coming from the computer's keyboard. The systems, which also scan for changes in the hardware and software since the previous time the computer booted up, can block access to sealed data if there are signs of tampering or if unauthorized software such as a virus tries to access cryptographic functions. And both Palladium and the Alliance scheme allow other similarly equipped computers to ask the system whether its machine is in a configuration they can trust; the chip always answers truthfully. This capability could allow a computer to query, say, an online banking site to make sure its security is satisfactory before starting an exchange of sensitive information. The overall goal, says Microsoft software architect Paul England, is to have computers "unconditionally protected against software attack."

But could the cure be worse than the disease? Proponents argue that the technology will at last keep data such as passwords, financial and medical records, and proprietary secrets safe from theft, while also preventing damage to computer networks from viruses and other software attacks. Critics, however, point out that the new chips can be used also to give software makers and content providers an unprecedented degree of control over users' machines. Opponents raise the specter of censorship of material on personal computers. They also warn about anticompetitive practices and draconian copyright enforcement through digital rights management. Trusted computing "could be good, could be bad," says Seth Schoen, at the Electronic Frontier Foundation, a nonprofit organization in San Francisco, CA. "It allows a lot of



BRIAN STAUFFER

Skeptics say the same technology that keeps passwords safe from theft will give software makers or governments the ability to control and censor consumers' hard drives.

things to happen, which in some sense couldn't have happened before."

Ross Anderson, a University of Cambridge computer scientist and an outspoken opponent of both plans, says trusted computing "can be useful, but it's a lot harder to do right than you might think." The systems could be used for remote detection and deletion of illegal software copies and even to exact payment each time a user plays a downloaded song, Anderson says. He also suggests that governments could use such features to actively censor documents and photos deemed politically sensitive or morally offensive: a state could require the chip to check online for valid licenses or lists of prohibited material and authorize it to delete data it deemed illicit.

Anderson and Schoen worry also that the new security technologies could be used to stifle competition. A maker of word processing software, for instance, could build in cryptographic keys other companies wouldn't have, preventing competitors' document formats from working on any machine that runs its software. That "would be a disadvantage for users," says Schoen. "But if a software publisher has a lot of market power, they can get away with including features that are a disadvantage to users."

Microsoft and the Alliance deny that their systems would restrict the kind of software or documents computer owners could use on their machines, and they emphasize that their only goal is to protect users' data. They also dismiss claims by critics who say the systems could be used for invasive procedures such as remote deletion of files. "The notes that I've seen posted on the Web, I think, were pretty farfetched and many of them impossible," says Clain Anderson, director of security solutions for IBM's PC division.

England at Microsoft, Meinschein at Intel, and Anderson at IBM all acknowledge, however, that the security chips will make digital rights management far more effective by allowing software makers and providers of online content including music, movies, and books to put more elaborate restrictions on the way computer owners use data. An operating system with a special security chip "could implement policy on top of it that users may like or that users may not like," says Meinschein.

The decision to buy a PC with such a security chip and even whether to enable the chip, however, will still belong to consumers, Meinschein notes. "We've taken, I think, the necessary initial steps to try to ensure that these technologies can be used in reasonable ways and that users have control of their privacy and of the device. But some of this is frankly going to be evolution, and we as users and as a community, we're going to have to work through this." Computer owners, in other words, will have to decide whether they really trust the good guys more than they fear the bad guys.
—Erika Jonietz

Chemical treatment renders a child's fingerprint readable.

CLEARER EVIDENCE

A household chemical rejuvenates faded fingerprints

FORENSICS | All fingerprints are *not* created equal. A print left by an adult can last for months, for instance, while those left by children are notoriously quick to degrade. But only recently has the chemistry behind these differences come to light, and scientists at the Y-12 National Security Complex, a National Nuclear Security Administration facility in Oak Ridge, TN, have devised a surprisingly simple chemical technique that renders even exceedingly faint prints more readable.

Good fingerprints, researchers at neighboring Oak Ridge National Laboratory discovered several years ago, are made primarily of sebum, the oil secreted by glands on the scalp, face, back, and chest. This material is transferred to the fingertips whenever a person touches his or her scalp or face, and it is transferred once again—as fingerprints—when the person touches a smooth surface. The fatty acids in sebum seal in moisture and give fingerprints longevity. By contrast, the worst fingerprints are left by those who have just washed their hands and by young children who have not yet begun to secrete sebum. Their fingerprints contain mainly salts and protein molecules dissolved in water, which dries up within hours, leaving virtually unreadable prints.

Last year Y-12 scientists Linda Lewis and Bob Smithwick discovered that by exposing such fingerprint ghosts to acetic acid, a chemical found in vinegar, they can regenerate the prints, making it possible to apply the chemical-fuming and dusting techniques employed to highlight and preserve good prints. Using their method, Lewis and Smithwick have revitalized previously unreadable prints after more than a month of dehydration.

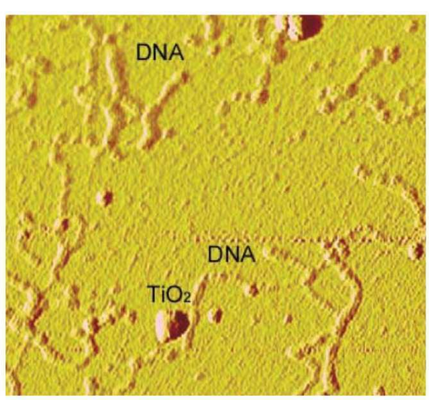
The acetic acid technique "may be a very viable method of regenerating older prints," says Bill Doyne, a forensic expert with the U.S. Army Criminal Investigation Laboratory. And for crime scene investigators, that find of a better method could be a boon that leads to more busts. —*Hank Schlesinger*

CRYSTAL THERAPY

NANOTECHNOLOGY | **One of the reasons gene therapy has faltered so far is that it's hard to get the right genes into cell nuclei safely. Genetically modified viruses are a common but less-than-ideal vehicle for the genes because the viruses can cause a fatal immune response. Looking for a way to deliver the genetic goods harmlessly and efficiently, cancer researcher Gayle Woloschak of Northwestern University Medical School and researchers at Argonne National Laboratory are turning to nanocrystals—particles a few billionths of a meter in diameter.**

The tiny particles act as "scaffolding" for the genetic material and make it possible to attach other molecules, such as peptides, that can help guide the complex directly to a cell's nucleus. In initial experiments, Woloschak and her coworkers used a small electrical stimulus to make the cell wall semipermeable, allowing the nanocrystals, which are only slightly wider than DNA, to slip through. Currently, the scientists are working on adding a navigational peptide to the scaffolding.

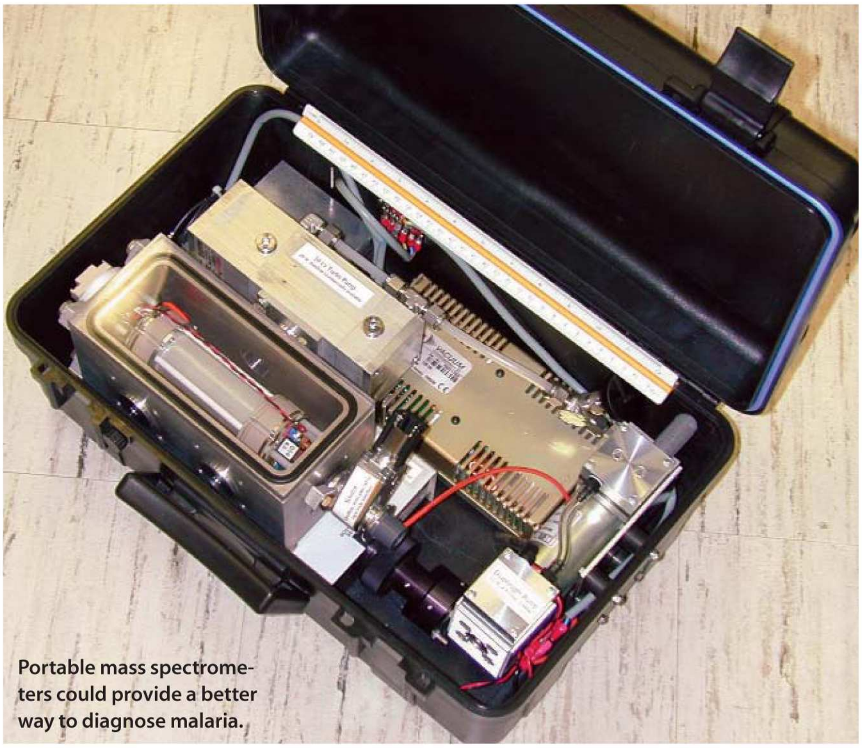
To make the crystals, Woloschak and her colleagues used titanium dioxide, a material that shouldn't provoke the immune system. Nanocrystals are attractive also because they can bear multiple genes, a property that could simplify therapy for diseases caused by several malfunctioning genes, Woloschak says. The nanocrystals may also provide a way to knock out unwanted genetic material, she adds. The researchers would attach to the nanoparticle a short stretch of DNA that matches a defective gene sequence; once bound with the unwanted genetic material in the cell, the nanoparticle could be broken apart by light or x-rays, thereby snipping out the problematic DNA.



Genes bound for ailing DNA hitch a ride on microscopic titanium dioxide (TiO_2) crystals.

Although Woloschak says the group's work is at least two years away from animal testing, nanoparticles' potential is definitely beginning to crystallize. "The hope is that nanoparticles will be able to incorporate some of the useful features of a viral vector, like the localization peptides, without the concern that they'll cause a negative immune reaction," says Daniel Feldheim, a North Carolina State University chemist who is developing gold nanoparticles that may also be enlisted in gene therapy efforts. —*Lisa Scanlon*

COURTESY OF ARGONNE NATIONAL LABORATORY (CRYSTAL THERAPY); COURTESY OF LINDA LEWIS (CLEARER EVIDENCE)



Portable mass spectrometers could provide a better way to diagnose malaria.

MASS SOLUTION

MEDICINE | Existing antibody-based tests for infectious diseases such as malaria are fairly cheap, but even a dollar per test can be prohibitively expensive if the target population comprises millions of people in the world's poorest countries. Now a better screening tool is coming to the fore: mass spectrometry, a common chemistry tool that precisely identifies molecules on the basis of their atomic weight. A portable machine built at Johns Hopkins University is more sensitive than antibody-based tests, covers all four kinds of malaria, and costs very little to operate.

That could make it a perfect tool for initial malaria screening of large populations, says Andrew Feldman, the physicist who developed the test at the Johns Hopkins University Applied Physics Laboratory in Laurel, MD. "My guess is we are going to be the gold standard for that kind of screening analysis," says Feldman, who is planning clinical trials. He found that a malarial by-product known as heme—an iron-containing molecule thrown off by the malaria-causing Plasmodium parasite as it "eats" hemoglobin—has a clear signature, which a mass spectrometer can recognize easily.

Unfortunately, although it is cheap to operate, the briefcase-size, 13-kilogram instrument currently costs about its weight in gold. Johns Hopkins has created a startup, Matrix Instrument, to manufacture it, but Feldman estimates that even produced in quantity, each unit would would tip the scales at $25,000. That sum, however hefty, might still be affordable for a mass-screening project.

Malarial screening is just one likely use for the new diagnostic tool. Using mass spectrometry, "you can detect many, many things with one instrument," says physical chemist Wayne Bryden, leader of the Johns Hopkins project that built the machine. Doctors who use the instrument don't even need to know what they are looking for; everything weighs something. Bryden hopes the malaria application will be the first step toward an all-purpose diagnostic device for hospital and health clinic settings—not to mention military applications such as sensing chemical- and biological-warfare agents. —*David Talbot*

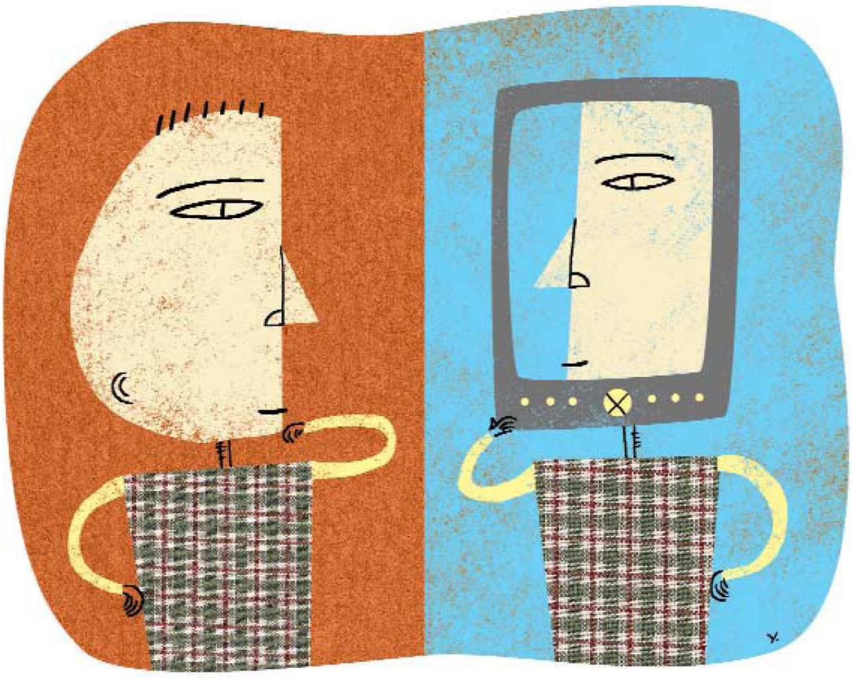
JAMES YANG (ILLUSTRATION); COURTESY OF JOHNS HOPKINS UNIVERSITY APPLIED PHYSICS LABORATORY (MASS SOLUTION)

WEALTHY WON'T WAIT

INTERNET | **Million-dollar customers who visit the Web page of, say, a brokerage house or an online merchant get the same response time—or delays—everybody else does. IBM, however, is putting finishing touches on a Web server management system that unabashedly separates the VIPs from the hoi polloi and can adapt itself to work on any combination of servers and operating systems.**

"Businesses want to differentiate customers so they can provide preferential treatment," says Donna Dillenberger, a computer scientist at IBM's Watson Research Center in Yorktown, NY. The software developed by her group responds to changing circumstances such as the ebb and flow of Internet traffic and the kinds of requests customers make. A big order or any order from a preferred customer, for instance, is always routed around bottlenecks and breakdowns to the least-loaded servers. "A business could say that people who order a Mercedes must get the order placed within three seconds. These would be more important than people who order bicycles," says Dillenberger.

Other companies offer Web traffic management systems for specific hardware, operating systems, and applications. But IBM says its system is the first that works across all configurations, thanks to its self-learning algorithms, which let it respond to new conditions and solve new problems autonomously. The concept of preferential treatment for big customers "is one that is starting to catch on," says Don LeClair, a vice president at Computer Associates in Islandia, NY. When the IBM system reaches the market later this year, it should take a load off loaded customers' minds.
—David Talbot



BRAINY RADIO

Researchers tune in on wireless devices that learn

WIRELESS | A personal digital assistant (PDA) falls from its owner's pocket during lunch. After a little while on the restaurant floor, it awakens, calls home, and notifies its owner that it has been left behind. That's all in a day's work for a "cognitive radio," a wireless device that's aware of its environment and learns from its user.

Cognitive radios don't exist yet. But Joseph Mitola, a computer scientist at Mitre, in Bedford, MA, aims to make them a reality by exploiting the added processing power that will be built into tomorrow's wireless devices. Mitola is one of the pioneers of "software radio," which gives users of cell phones and other two-way radios the ability to use a single device to communicate over a range of frequencies. Now Mitola is thinking about other applications—such as artificial-intelligence-based learning—for wireless devices stuffed with software. "A cognitive radio learns the preferences of its user without being explicitly programmed," Mitola says.

As a first step, Mitola has customized a simulated PDA to glean owner preferences from text-based information. To learn from other kinds of patterns, wireless devices need a standardized way to describe and track such factors as location and transmission conditions, so Mitola has crafted a computer language that will do just that. Before sending data to the home office of a cost-conscious enterprise, for instance, a cognitive PDA with software written in Mitola's new language might automatically search for a cheap wide-area-network connection before it would use a more expensive cellular network. Mitola is also working with the U.S. Defense Advanced Research Projects Agency to spot promising applications in areas such as battlefield radios that can detect and outmaneuver jamming attempts. He cautions, though, that it could take a decade for handheld devices to gain enough processor power and memory to achieve cognition on this scale.

Cognitive radio eventually will benefit both military and commercial carriers, believes Jeffrey Reed, deputy director of Virginia Polytechnic Institute's Mobile and Portable Radio Research Group, whose investigators are studying ways networks of cognitive radios might interact. Wireless providers, especially, will need machine-driven ways to guide customers through the panoply of options for voice and data communication for so-called fourth-generation, or 4G, wireless services. Says Reed, "I think this is where 4G is going." —*Joab Jackson*

I FEEL YOUR PLANE

INTERFACES | **In today's highly complex airplane cockpits, pilots can have trouble keeping up with information flow, especially if they become disoriented in an emergency. But at the Institute for Human and Machine Cognition at the University of West Florida, a newly developed wearable interface lets pilots use their sense of touch to complement audiovisual navigation cues. The tactile displays "reduce the pilot's workload to free up more gray matter for other tasks," says principal investigator Anil Raj.**

In collaboration with the U.S. Navy, Raj has developed networks of tiny vibrators that may be strapped to a pilot's torso, connected to navigation sensors and signal-processing software, and activated by streams of pressurized air. If an aircraft is turning left, say, its pilot feels a buzz on his or her left side. The system can also warn pilots about deviations from course or approaching threats; intense buzzing against the pilot's back could signify an enemy plane behind the aircraft.

Raj's prototypes have proved effective in flight tests, says Angus Rupert, director of Spatial Orientation Systems at the Naval Aerospace Medical Research Laboratory. The Navy will use the technology in helicopter missions by special-operations troops as early as this spring, he adds. For the pilots, the bottom line is heightened spatial awareness and fewer accidents—even if they feel as if they are flying by the seat of their pants. —*Gregory T. Huang*

Networked "tactors" convey spatial information by vibrating against pilots' skin.

SLIMFILMS (I FEEL YOUR PLANE); JAMES YANG (ILLUSTRATION)

SIMSON GARFINKEL

THE NET EFFECT

THE FREE-SOFTWARE IMPERATIVE

You have a moral obligation to use free software. At least, that's the message that Patrick Ball is trying to get out.

Ball is deputy director of the Science and Human Rights Program of the American Association for the Advancement of Science. He's best known for his analysis of the Kosovo refugee movements during NATO's bombing campaign in 1999. Now Ball is on another kind of mission: he's telling the world's 10,000 human-rights groups to stop using pirated copies of Microsoft Windows and Microsoft Office and trying to persuade them to use free software instead.

The best-known examples of free software are the GNU/Linux-based operating system and OpenOffice—an application suite that includes a decent word processor, spreadsheet, and presentation package. You can legally make as many copies of these programs as you want. Moreover, because this software is distributed with its source code, any programmer can examine the code, fix bugs, and tinker with the software's features.

Unlike some other advocates of free software, Ball is not fundamentally opposed to Microsoft or other commercial-software makers. But he worries that too many people put themselves in jeopardy by illegally copying programs from these companies. Ball is especially concerned about overseas human-rights organizations, but his argument is universal.

Illegal software copies are particularly common in poor countries. The rate is highest in Vietnam, where the Business Software Alliance estimates 94 percent of all software used in 2001 was illicitly copied. But bootlegging is common in disadvantaged parts of the United States too. In Mississippi, 49 percent of the software now in use runs afoul of copyright laws.

Such copying poses a special risk to human rights organizations: U.S. companies and the U.S. government are working hard to make this practice a go-to-jail offense worldwide, as it is in the United States. Although the world frowns on countries that lock up their citizens for crimes of conscience, it's easy to imagine that some repressive third-world regime could invoke antipiracy laws as grounds for shutting down a meddlesome human-rights organization. And if U.S. or other Western governments object, the regime might logically respond, "You are always telling us we should be more aggressive in the protection of intellectual property. And now when we are, you criticize us."

Would Amnesty International mount a letter-writing campaign to get a human rights activist out of jail if she had been arrested for pirating Microsoft Word? Probably not, says Ball. Amnesty International, the world's richest human-rights group, buys properly licensed copies of Microsoft Office for its computers. But when rich organizations use expensive, proprietary software, they implicitly encourage the poorer organizations with whom they work and share documents to do the same. And that requires either violating the law or using scarce resources to buy legitimate software. This is a compelling reason to push for the widespread adoption of free software. The pervasive use of Microsoft Office, combined with a staunch antipiracy program, amounts to economic colonialism.

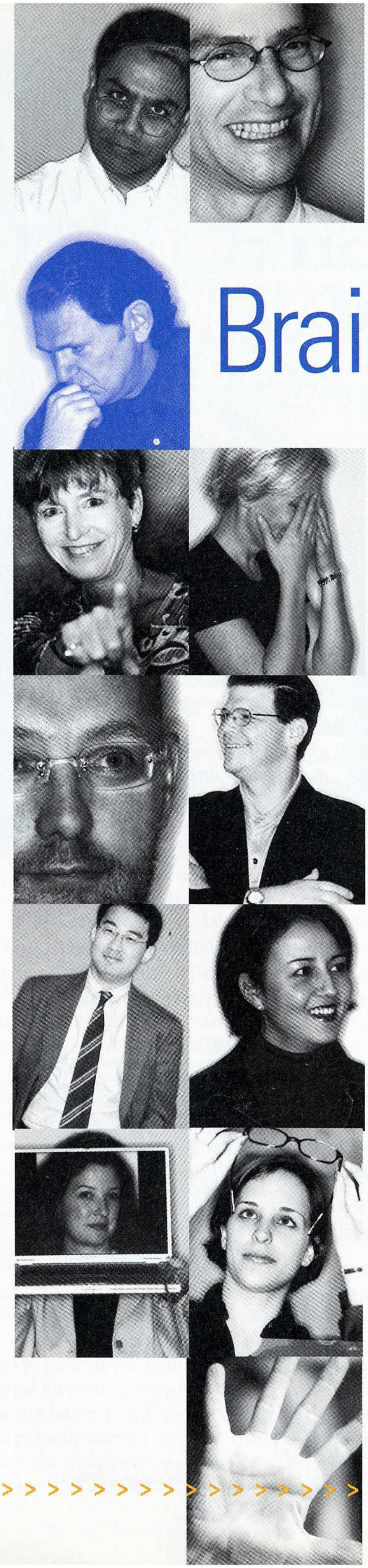
There is another reason for human rights organizations to eschew Windows: verifiability. Whenever death squads make threats against a villager who speaks with rights workers, those workers have a moral responsibility to be sure their computers are secured with the best technology available. Lives depend on it. There is no way to verify the security of Windows: the software is secret. Indeed, Microsoft's latest license agreements give the company the right to go into computers without their owners' permission (or knowledge) to load software and retrieve "technical" information at Microsoft's sole discretion. A hostile government could probably exploit these vulnerabilities, reaching through the Internet to break into a rights worker's computer, never even setting foot in that person's office.

Illegal software copies pose a special risk to human rights organizations. Amnesty International probably would not campaign to free an activist who was arrested for pirating Microsoft Word.

The only way a human rights organization (or anybody else) can be sure there are no back doors into its software is to have an expert remove all parts of the program that allow remote access. Clearly, this verification would require access to the source code. In practice, the need for verification rules out not only Windows but also any other closed-source system, including those on Macintoshes and on Palm handheld devices.

Even two years ago, it wasn't practical for nongeeks to run Linux and the rest of the free-software mélange. (Articles in computer magazines that claimed otherwise were prematurely enthusiastic.) But today, thanks to Red Hat Software and OpenOffice, free software is a viable alternative. The current version of Red Hat Linux runs on a wide range of hardware, automatically loads OpenOffice, and provides a usable and visually attractive desktop.

There's another reason for my becoming more bullish about free software. A few months ago, a system administrator in a Central American human-rights office e-mailed Ball that the office had stopped running its pirated copy of Microsoft Exchange and had switched its e-mail system to Red Hat Linux. The reason: it was nearly impossible to run Exchange without expensive books and training courses. Free software, by contrast, comes with free documentation. And monetary freedom translates into political freedom by eliminating at least one way oppressive governments can thwart these groups' good works. TR



MIT'S MAGAZINE OF INNOVATION
TECHNOLOGY REVIEW
FEBRUARY 2003

In labs around the world, researchers are busy creating technologies that will change the way we conduct business and live our lives. These are not the latest crop of gadgets and gizmos: they are completely new technologies that could soon transform computing, medicine, manufacturing, transportation, and our energy infrastructure. Nurturing the people and the culture needed to make the birth of such technological ideas possible is a messy endeavor, as MIT Media Lab cofounder Nicholas Negroponte explains on page 34. But in this special issue, *Technology Review*'s editors have identified 10 emerging technologies that we predict will have a tremendous influence in the near future. For each, we've chosen a researcher or research team whose work and vision is driving the field. The profiles, which begin on page 36, offer a sneak preview of the technology world in the years and decades to come.

10 EMERGING TECHNOLOGIES THAT WILL CHANGE THE WORLD

Creating a Culture of Ideas

What sparks the ideas that beget new technologies? The cofounder of MIT's Media Lab says celebrating wrong answers and listening to youth make a good start.

BY NICHOLAS NEGROPONTE

Innovation is inefficient. More often than not, it is undisciplined, contrarian, and iconoclastic; and it nourishes itself with confusion and contradiction. In short, being innovative flies in the face of what almost all parents want for their children, most CEOs want for their companies, and heads of states want for their countries. And innovative people are a pain in the ass.

Yet without innovation we are doomed—by boredom and monotony—to decline. So what makes innovation happen, and just where do new ideas come from? The basic answers—providing a good educational system, encouraging different viewpoints, and fostering collaboration—may not be surprising. Moreover, the ability to fulfill these criteria has served the United States well. But some things—the nature of higher education among them—will have to change in order to ensure a perpetual source of new ideas.

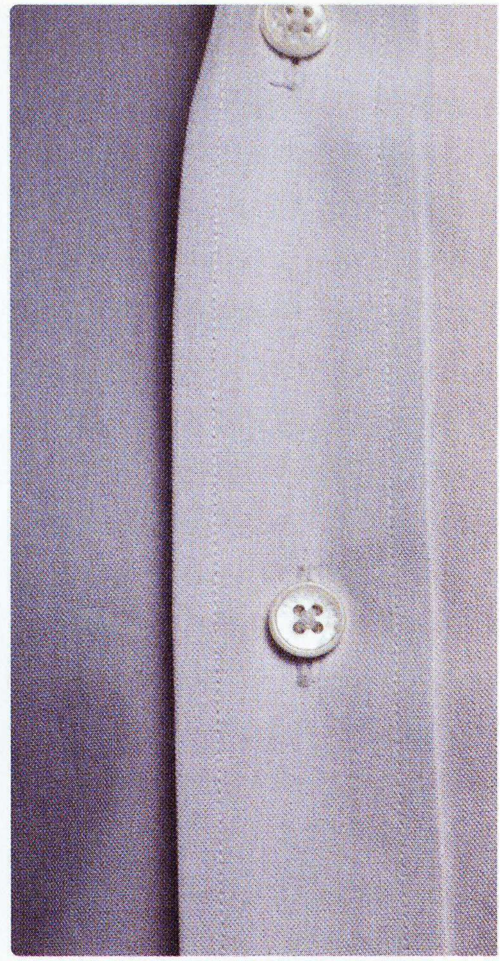
One of the basics of a good system of innovation is diversity. In some ways, the stronger the culture (national, institutional, generational, or other), the less likely it is to harbor innovative thinking. Common and deep-seated beliefs, widespread norms, and behavior and performance standards are enemies of new ideas. Any society that prides itself on being harmonious and homogeneous is very unlikely to catalyze idiosyncratic thinking. Suppression of innovation need not be overt. It can be simply a matter of people's walking around in tacit agreement and full comfort with the status quo.

A very heterogeneous culture, by contrast, breeds innovation by virtue of its people, who look at everything from different viewpoints. America, the so-called melting pot, is seen by many as having no culture (with either a capital *C* or a lowercase *c*). In rankings of students in industrial countries, U.S. high school students come across as average, at best, in reading, mathematics, and science. And unfortunately, the nation is unrivaled in gun-related crimes among young people. Yet, looking back over the past century, the United States has accounted for about a third of all Nobel prizes and has produced an unrivaled outpouring of innovations—from factory automation to the integrated circuit and gene splicing—that are the backbone of worldwide economic growth.

I see two reasons for this. One is that we do not stigmatize those who have tried and been unsuccessful. In fact, many venture capitalists are more, not less, likely to invest in somebody who has failed with an earlier startup than in someone who is launching his or her first company. The real disappointment is when people do not learn from their mistakes.

The other reason is that we are uniquely willing to listen to our young. In many cultures, age carries too much weight. Experience is rewarded over imagination, and respect can be too deferential. In some cultures, people are given jobs on the basis of age, creating a sedentary environment stifling to the young. Remember the saying "Children are to be seen and not heard"? Well, look at the economic growth created by such "children" as Bill Gates and Michael Dell, to name just two.

That's the good news. But when it comes to nurturing our youth, we have to do better. I am especially concerned about early education, which can (and usually does) have a profoundly negative effect on creativity. In the race to understand what children learn, we are far too enthusiastic about celebrating their successes. What is more fascinating is what children do wrong. Even the concept of "wrong" should get some attention. Though the wind is not made by leaves flapping, as



some children guess, the theory is sufficiently profound that it should not be dismissed out of hand. In fact, disassembling erroneous concepts is one of the best ways to find new ideas. The process is akin to debugging a computer program and has almost nothing to do with drill and practice (which is once again becoming a cornerstone of schooling).

Our biggest challenge in stimulating a creative culture is finding ways to encourage multiple points of views. Many engineering deadlocks have been broken by people who are not engineers at all. This is simply because perspective is more important than IQ. The irony is that perspective will not get kids into college, nor does it help them thrive there. Academia rewards depth. Expertise is bred by experts who work with their own kind. Departments and labs focus on fields and subfields, now and then adding or subtracting a domain. Graduate degrees, not to mention tenure, depend upon tunneling into truths and illuminating ideas in narrow areas.

The antidote to such canalization and compartmentalization is being interdisciplinary, a term that is at once utterly banal

FREDRIK BRODÉN

and, in advanced studies, describes an almost impossible goal. Interdisciplinary labs and projects emerged in the 1960s to address big problems spanning the frontiers of the physical and social sciences, engineering, and the arts. The idea was to unite complementary bodies of knowledge to address issues that transcended any one skill set. Fine. Only recently, however, have people realized that interdisciplinary approaches can bring enormous value to some very small problems and that interdisciplinary environments also stimulate creativity. In maximizing the differences in backgrounds, cultures, ages, and the like, we increase the likelihood that the results will not be what we had imagined.

Two additional ingredients are needed to cultivate new ideas. Both have to do with maximizing serendipity. First, we need to encourage risk. This is particularly hard in midcareer and often flies in the face of peer review and the mechanisms for corporate advancement. This is simply because risk, on its own, can look pretty stupid. People who look around corners are exposed to failure and ridicule, and thus they must find buoyancy, or support, within their own environment. If they don't, counterintuitive ideas will remain so.

The second ingredient is encouragement for openness and idea sharing—another banality nearly impossible to achieve. At the digital bubble's peak, being open about ideas was particularly hard for computer scientists because people saw riches coming from *not* sharing their ideas. Students would withhold ideas until after graduation. As one person held his or her cards close, another followed, and as a result, many research labs declined in value and effectiveness. In this regard, thank God the bubble has burst.

Not so many years ago, Bell Labs conducted so much research it could easily house some very high-risk programs, including the so-called blue-sky thinking that led to information theory and the discovery of the cosmic microwave background radiation. But the world benefited, and sometimes AT&T did too.

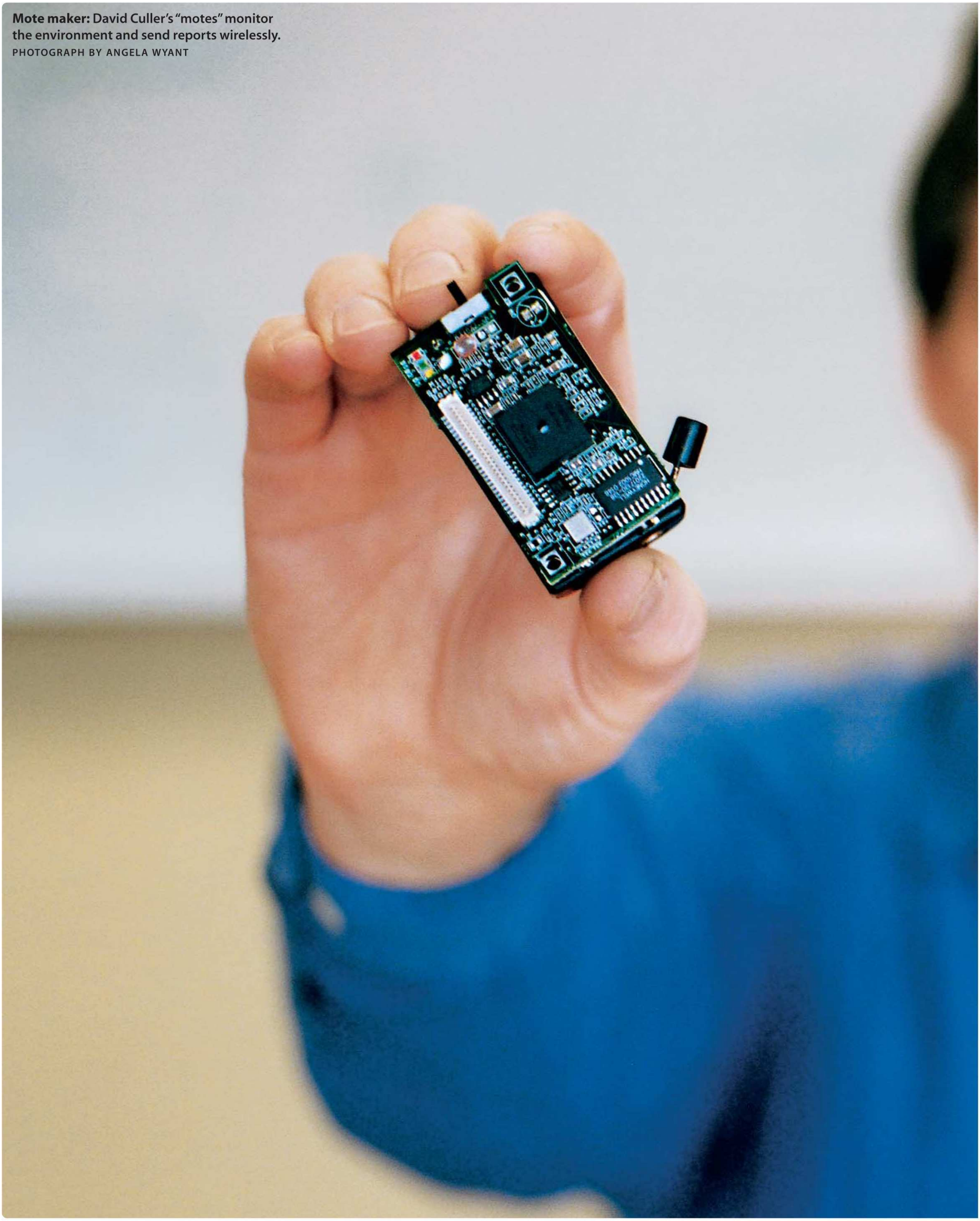
Now, Bell Labs is a shadow of its former self, subdivided several times through AT&T's 1984 divestiture and subsequent split into Lucent, NCR, and the parent firm. Moreover, it is not alone. As the economy sags and companies trim their expenses, some of the first cuts are in high-risk or open-ended research programs. Even if the research budget does not drop, the nature of projects is prone to be more developmental than really innovative. If the trend continues, eventually we will suffer a deficit of new ideas. Already, fewer and fewer big corporations are focusing on new ideas. And the formation of startups has come almost to a standstill.

More than ever before, in the new "new economy," research and innovation will need to be housed in those places where there are parallel agendas and multiple means of support. Universities, suitably reinvented to be interdisciplinary, can fit this profile because their other "product line," besides research, is people. When research and learning are combined, far greater risks can be taken and the generation of ideas can be less efficient. Right now, only a handful of U.S. universities constitute such "research universities." More will have to become so. Universities worldwide will have to follow.

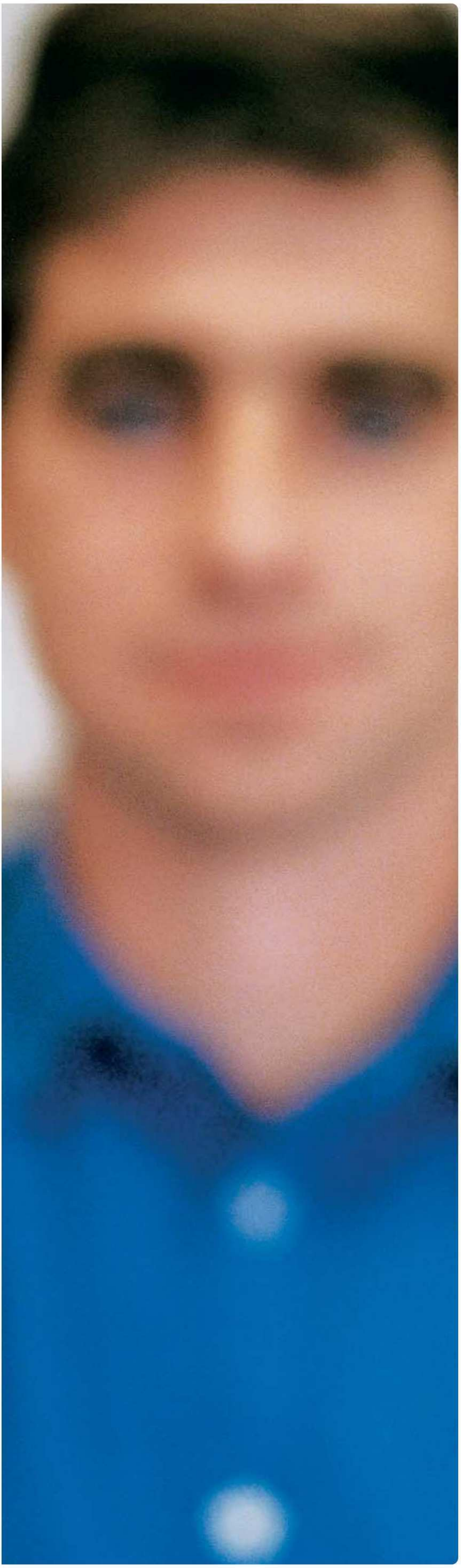
Industry can outsource basic research, just as it does many other operations. That means innovation has to become a precompetitive phenomenon—something Japan understood in the early 1980s, when its Ministry of International Trade and Industry (now the Ministry of Economy, Trade, and Industry) funded Japanese companies' collaboration on robotics, artificial intelligence, and semiconductor manufacturing. While this approach does not always work, it can be far more effective than most companies assume. Costs are shared, different viewpoints are nourished, and innovation stands a chance for survival in even the worst economic times.

The ability to make big leaps of thought is a common denominator among the originators of breakthrough ideas. Usually this ability resides in people with very wide backgrounds, multidisciplinary minds, and a broad spectrum of experiences. Family influences, role models, travel, and living in diverse settings are obvious contributors, as are educational systems and the way cultures value youth and perspective. As a society, we can shape some of these. Some we can't. A key to ensuring a stream of big ideas is accepting these messy truths about the origin of ideas and continuing to reward innovation and celebrate emerging technologies.

Ten follow. TR



Mote maker: David Culler's "motes" monitor the environment and send reports wirelessly.
PHOTOGRAPH BY ANGELA WYANT



DAVID CULLER

Wireless Sensor Networks

Great Duck Island, a 90-hectare expanse of rock and grass off the coast of Maine, is home to one of the world's largest breeding colonies of Leach's storm petrels—and to one of the world's most advanced experiments in wireless networking. Last summer, researchers bugged dozens of the petrels' nesting burrows with small monitoring devices called motes. Each is about the size of its power source—a pair of AA batteries—and is equipped with a processor, a tiny amount of computer memory, and sensors that monitor light, humidity, pressure, and heat. There's also a radio transceiver just powerful enough to broadcast snippets of data to nearby motes and pass on information received from other neighbors, bucket brigade–style.

This is more than the latest in avian intelligence gathering. The motes preview a future pervaded by networks of wireless battery-powered sensors that monitor our environment, our machines, and even *us*. It's a future that David Culler, a computer scientist at the University of California, Berkeley, has been working toward for the last four years. "It's one of the big opportunities" in information technology, says Culler. "Low-power wireless sensor networks are spearheading what the future of computing is going to look like."

Culler is on partial leave from Berkeley to direct an Intel "lablet" that is perfecting the motes, as well as the hardware and software systems needed to clear the way for wireless networks made up of thousands or even millions of sensors. These networks will observe just about everything, including traffic, weather, seismic activity, the movements of troops on battlefields, and the stresses on buildings and bridges—all on a far finer scale than has been possible before.

Because such networks will be too distributed to have the sensors hard-wired into the electrical or communications grids, the lablet's first challenge was to make its prototype motes communicate wirelessly with minimal battery power. "The devices have to organize themselves in a network by listening to one another and figuring out who can they hear...but it costs power to even listen," says Culler. That meant finding a way to leave the motes' radios off most of the time and still allow data to hop through the network, mote by mote, in much the same way that data on the Internet are broken into packets and routed from node to node.

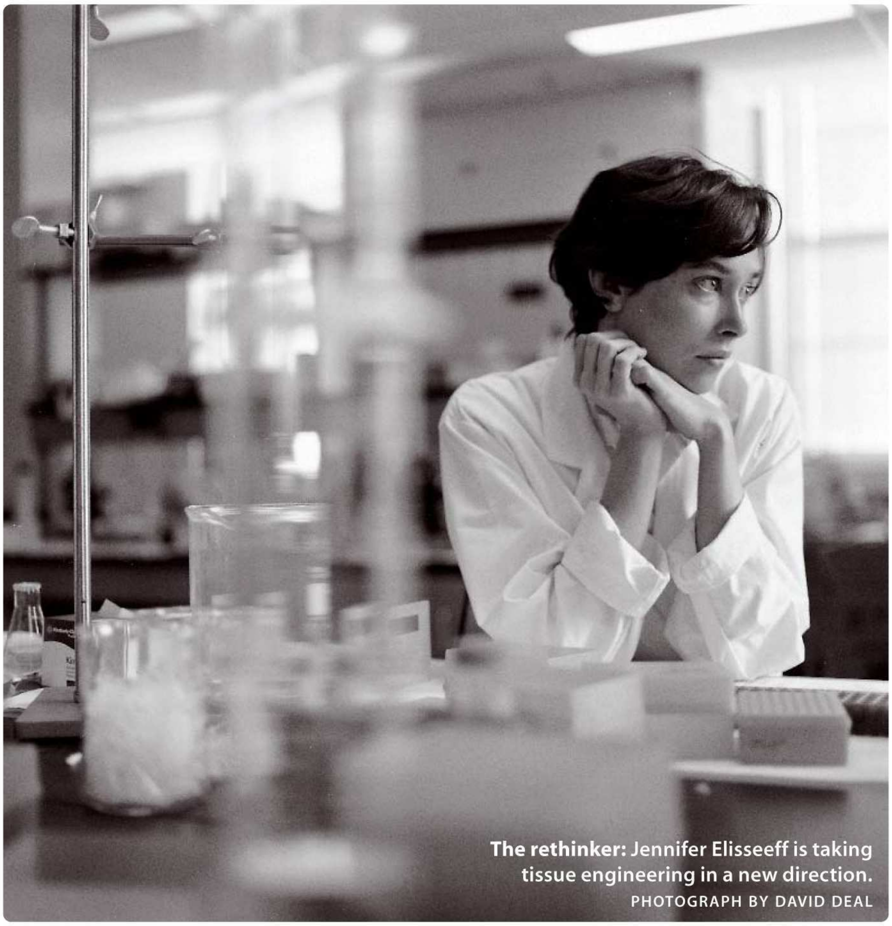
Until Culler's group attacked the problem, wireless networking had lacked an equivalent to the data-handling protocols that make the Internet work. The lablet's solution: TinyOS, a compact operating system only a few kilobytes in size, that handles such administrative tasks as encoding data packets for relay and turning on radios only when they're needed. The motes that run TinyOS should cost a few dollars apiece when mass produced and are being field-tested in several locations from Maine to California, where Berkeley seismologists are using them to monitor earthquakes.

Anyone is free to download and tinker with TinyOS, so researchers outside of Berkeley and Intel can test wireless sensor networks in a range of environments without having to reinvent the underlying technology. Culler's motes have been "a tremendously enabling platform," says Deborah Estrin, director of the Center for Embedded Networked Sensing at the University of California, Los Angeles. Estrin is rigging a nature reserve in the San Jacinto mountains with a dense array of wireless microclimate and imaging sensors.

Others are trying to make motes even smaller. A group led by Berkeley computer scientist Kristofer Pister is aiming for one cubic millimeter—the size of a few dust mites. At that scale, wireless sensors could permeate highway surfaces, building materials, fabrics, and perhaps even our bodies. The resulting data bonanza could vastly increase our understanding of our physical environment—and help us protect our own nests. —*Wade Roush*

OTHERS IN WIRELESS SENSOR NETWORKS

RESEARCHER	PROJECT
Gaetano Borriello U. Washington; Intel	Small embedded computers and communications protocols
Deborah Estrin U. California, Los Angeles	Networking, middleware, data handling, and hardware for distributed sensors and actuators
Michael Horton Crossbow Technology	Manufacture of sensors and motes
Kristofer Pister U. California, Berkeley	Millimeter-size sensing and communication devices



The rethinker: Jennifer Elisseeff is taking tissue engineering in a new direction.
PHOTOGRAPH BY DAVID DEAL

JENNIFER ELISSEEFF

Injectable Tissue Engineering

Every year, more than 700,000 patients in the United States undergo joint replacement surgery. The procedure—in which a knee or a hip is replaced with an artificial implant—is highly invasive, and many patients delay the surgery for as long as they can. Jennifer Elisseeff, a biomedical engineer at Johns Hopkins University, hopes to change that with a treatment that does away with surgery entirely: injectable tissue engineering. She and her colleagues have developed a way to inject joints with specially designed mixtures of polymers, cells, and growth stimulators that solidify and form healthy tissue. "We're not just trying to improve the current therapy," says Elisseeff. "We're really trying to change it completely."

Elisseeff is part of a growing movement that is pushing the bounds of tissue engineering—a field researchers have long hoped would produce lab-grown alternatives to transplanted organs and tissues. For the last three decades, researchers have focused on growing new tissues on polymer scaffolds in the lab. While this approach has had success producing small amounts of cartilage and skin, researchers have had difficulty keeping cells alive on larger scaffolds. And even if those problems could be worked out, surgeons would still have to implant the lab-grown tissues. Now, Elisseeff, as well as other academic and industry researchers, are turning to injectable systems that are less invasive and far cheaper. Many of the tissue-engineering applications to reach the market first could be delivered by syringe rather than implants, and Elisseeff is pushing to make this happen as soon as possible.

Elisseeff and her colleagues have used an injectable system to grow cartilage in mice. The researchers added cartilage cells to a light-sensitive liquid polymer and injected it under the skin on the backs of mice. They then shone ultraviolet light through the skin, causing the polymer to harden and encapsulate the cells. Over time, the cells multiplied and developed into cartilage. To test the feasibility of the technique for minimally invasive surgery, the researchers injected the liquid into the knee joints of cadavers. The surgeons used a fiber-optic tube to view the hardening process on a television monitor. "This has huge implications," says James Wenz, an orthopedic surgeon at Johns Hopkins who is collaborating with Elisseeff.

While most research on injectable systems has focused on cartilage and bone, observers say this technology could be extended to tissues such as those of the liver and heart. The method could be used to replace diseased portions of an organ or to enhance its functioning, says Harvard University pediatric surgeon Anthony Atala. In the case of heart failure, instead of opening the chest and surgically implanting an engineered valve or muscle tissue, he says, simply injecting the right combination of cells and signals might do the trick.

For Elisseeff and the rest of the field, the next frontier lies in a powerful new tool: stem cells. Derived from sources like bone marrow and embryos, stem cells have the ability to differentiate into numerous types of cells. Elisseeff and her colleagues have exploited that ability to grow new cartilage and bone simultaneously—one of the trickiest feats in tissue engineering. They made layers of a polymer-and-stem-cell mixture, infusing each layer with specific chemical signals that triggered the cells to develop into either bone or cartilage. Such hybrid materials would simplify knee replacement surgeries, for instance, that require surgeons to replace the top of the shin bone and the cartilage above it.

Don't expect tissue engineers to grow entire artificial organs anytime soon. Elisseeff, for one, is aiming for smaller advances that will make tissue engineering a reality within the decade. For the thousands of U.S. patients who need new joints every year, such small feats could be huge. *—Alexandra M. Goho*

OTHERS IN INJECTABLE TISSUE ENGINEERING

RESEARCHER	PROJECT
Anthony Atala Harvard Medical School	Cartilage
Jim Burns Genzyme	Cartilage
Antonios Mikos Rice U.	Bone and cardiovascular tissue
David Mooney U. Michigan	Bone and cartilage

PAUL ALIVISATOS

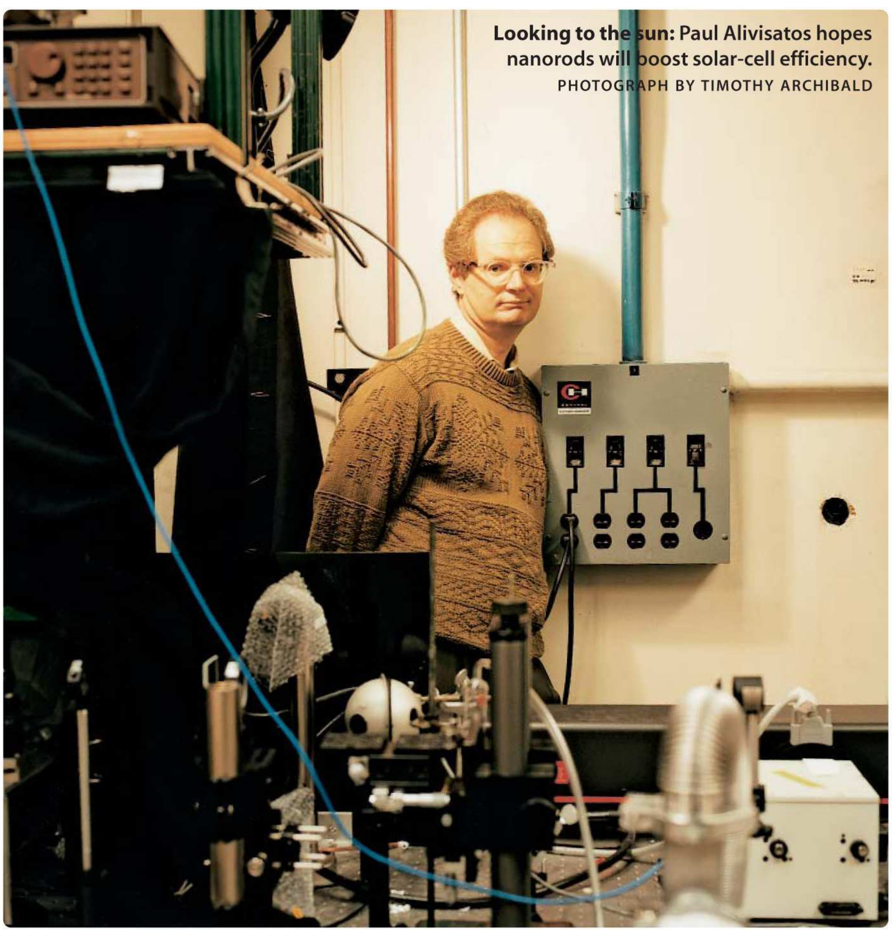
Nano Solar Cells

The sun may be the only energy source big enough to wean us off fossil fuels. But harnessing its energy depends on silicon wafers that must be produced by the same exacting process used to make computer chips. The expense of the silicon wafers raises solar-power costs to as much as 10 times the price of fossil fuel generation—keeping it an energy source best suited for satellites and other niche applications.

Paul Alivisatos, a chemist at the University of California, Berkeley, has a better idea: he aims to use nanotechnology to produce a photovoltaic material that can be spread like plastic wrap or paint. Not only could the nano solar cell be integrated with other building materials, it also offers the promise of cheap production costs that could finally make solar power a widely used electricity alternative.

Alivisatos's approach begins with electrically conductive polymers. Other researchers have attempted to concoct solar cells from these plastic materials *(see "Solar on the Cheap," TR January/February 2002)*, but even the best of these devices aren't nearly efficient enough at converting solar energy into electricity. To improve the efficiency, Alivisatos and his coworkers are adding a new ingredient to the polymer: nanorods, bar-shaped semiconducting inorganic crystals measuring just seven nanometers by 60 nanometers. The result is a cheap and flexible material that could provide the same kind of efficiency achieved with silicon solar cells. Indeed, Alivisatos hopes that within three years, Nanosys—a Palo Alto, CA, startup he cofounded—will roll out a nanorod solar cell that can produce energy with the efficiency of silicon-based systems.

The prototype solar cells he has made so far consist of sheets of a nanorod-polymer composite just 200 nanometers thick. Thin layers of an electrode sandwich the composite sheets. When sunlight hits the sheets, they absorb photons, exciting electrons in the polymer and the nanorods, which make up 90 percent of the composite. The result is a useful current that is carried away by the electrodes.



Looking to the sun: Paul Alivisatos hopes nanorods will boost solar-cell efficiency.
PHOTOGRAPH BY TIMOTHY ARCHIBALD

Early results have been encouraging. But several tricks now in the works could further boost performance. First, Alivisatos and his collaborators have switched to a new nanorod material, cadmium telluride, which absorbs more sunlight than cadmium selenide, the material they used initially. The scientists are also aligning the nanorods in branching assemblages that conduct electrons more efficiently than do randomly mixed nanorods. "It's all a matter of processing," Alivisatos explains, adding that he sees "no inherent reason" why the nano solar cells couldn't eventually match the performance of top-end, expensive silicon solar cells.

The nanorod solar cells could be rolled out, ink-jet printed, or even painted onto surfaces, so "a billboard on a bus could be a solar collector," says Nanosys's director of business development, Stephen Empedocles. He predicts that cheaper materials could create a $10 billion annual market for solar cells, dwarfing the growing market for conventional silicon cells.

Alivisatos's nanorods aren't the only technology entrants chasing cheaper solar power. But whether or not his approach eventually revolutionizes solar power, he is bringing novel nanotechnology strategies to bear on the problem. And that alone could be a major contribution to the search for a better solar cell. "There will be other research groups with clever ideas and processes—maybe something we haven't even thought of yet," says Alivisatos. "New ideas and new materials have opened up a period of change. It's a good idea to try many approaches and see what emerges."

Thanks to nanotechnology, those new ideas and new materials could transform the solar cell market from a boutique source to the Wal-Mart of electricity production. —*Eric Scigliano*

OTHERS IN NANO SOLAR CELLS

RESEARCHER	PROJECT
Richard Friend U. Cambridge	Fullerene-polymer composite solar cells
Michael Grätzel Swiss Federal Institute of Technology	Nanocrystalline dye-sensitized solar cells
Alan Heeger U. California, Santa Barbara	Fullerene-polymer composite solar cells
N. Serdar Sariciftci Johannes Kepler U.	Polymer and fullerene-polymer composite solar cells

ROLF ISERMANN

Mechatronics

To improve everything from fuel economy to performance, automotive researchers are turning to "mechatronics," the integration of familiar mechanical systems with new electronic components and intelligent-software control. Take brakes. In the next five to 10 years, electromechanical actuators will replace hydraulic cylinders; wires will replace brake fluid lines; and software will mediate between the driver's foot and the action that slows the car. And because lives will depend on such mechatronic systems, Rolf Isermann, an engineer at Darmstadt University of Technology in Darmstadt, Germany, is using software that can identify and correct for flaws in real time to make sure the technology functions impeccably. "There is a German word for it: *gründlich*," he says. "It means you do it *really* right."

In order to do mechatronic braking right, Isermann's group is developing software that tracks data from three sensors: one detects the flow of electrical current to the brake actuator; a second tracks the actuator's position; and the third measures its clamping force. Isermann's software analyzes those numbers to detect faults—such as an increase in friction—and flashes a dashboard warning light, so the driver can get the car serviced before the fault leads to failure.

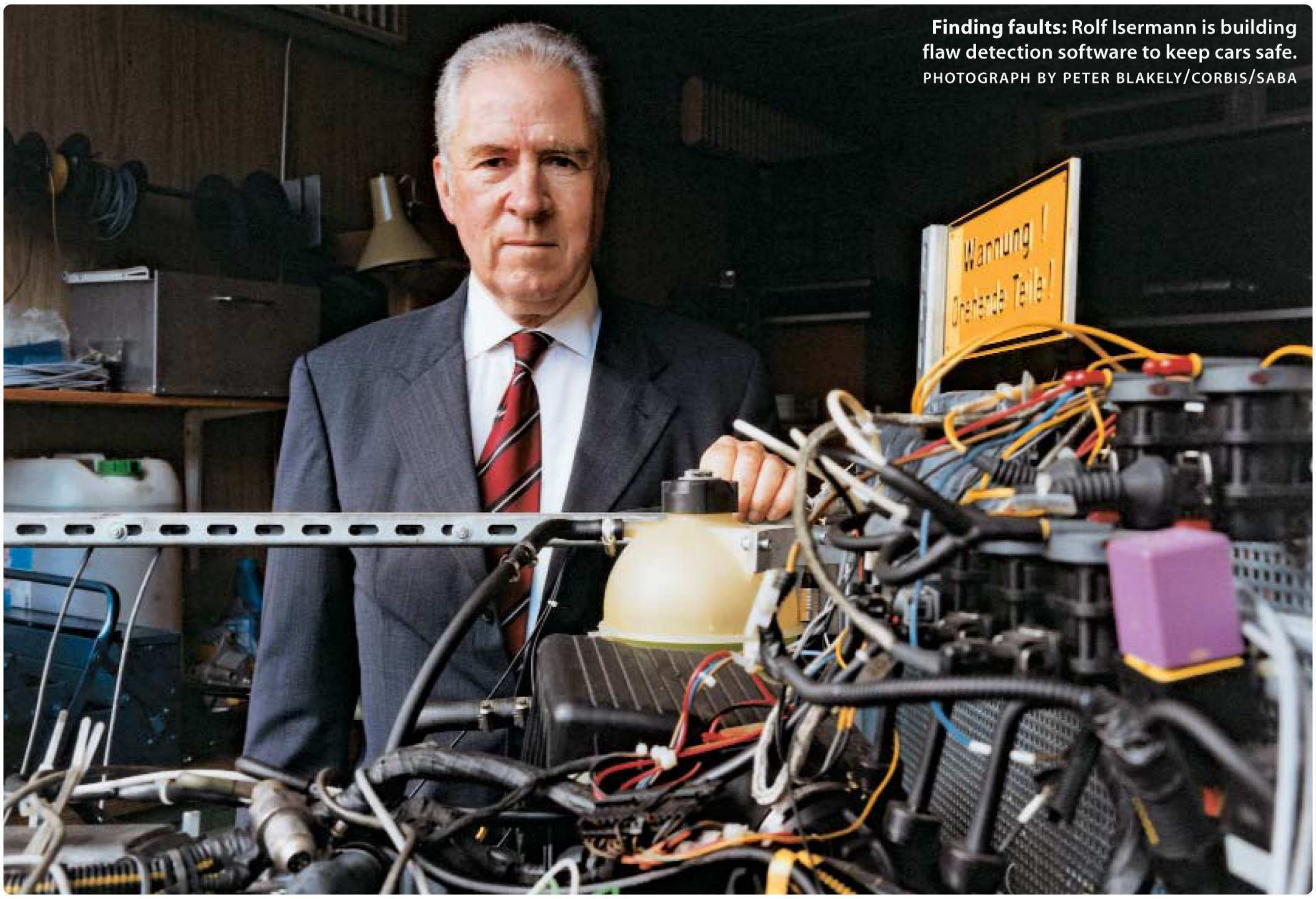
"Everybody initially was worried about the safety of electronic devices. I think people are now becoming aware they are safer than mechanical ones," says Karl Hedrick, a mechanical engineer at the University of California, Berkeley. "A large part of the reason they are safer is you can build in fault diagnoses and fault tolerance. Isermann is certainly in the forefront of people developing technology to do this."

Isermann is also working to make engines run cleaner. He is developing software that detects combustion misfires, which can damage catalytic converters and add to pollution. Because it's not practical to have a sensor inside a combustion chamber, Isermann's system relies on data from sensors that measure oxygen levels in exhaust and track the speed of the crankshaft (the mechanism that delivers the engine's force to the wheels). Tiny fluctuations in crankshaft speed accompanied by changes in emissions reveal misfires. If a misfire is detected, the software can warn the driver or, in the future, might automatically fix the problem.

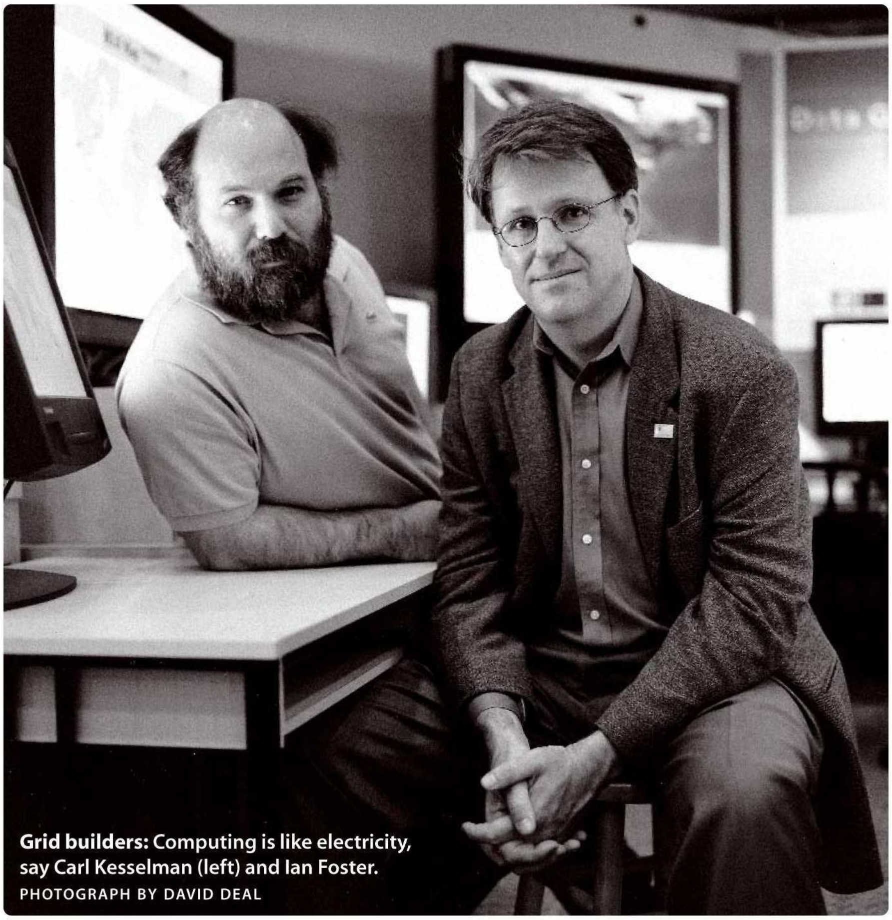
Partnerships with manufacturing companies—including DaimlerChrysler and Continental Teves—merge the basic research from Isermann's group with industry's development of such technologies in actual cars. Isermann says that "80 to 90 percent of the innovations in the development of engines and cars these

OTHERS IN MECHATRONICS

RESEARCHER	PROJECT
Lino Guzzella Swiss Federal Institute of Technology	Engine modeling and control systems
Karl Hedrick and Masayoshi Tomizuka U. California, Berkeley	Control systems and theory
Uwe Kiencke U. Karlsruhe	Digital signal processing
Philip Koopman Carnegie Mellon U.	Fault tolerance in control software
Lars Nielsen Linköping U.	Engine control systems



Finding faults: Rolf Isermann is building flaw detection software to keep cars safe.
PHOTOGRAPH BY PETER BLAKELY/CORBIS/SABA



Grid builders: Computing is like electricity, say Carl Kesselman (left) and Ian Foster.
PHOTOGRAPH BY DAVID DEAL

days are due to electronics and mechatronics." Until recent years, mechatronic systems were found mainly in such big-ticket items as aircraft and industrial equipment or in small precision components for products such as cameras and photocopiers. But new applications in cars and trucks have helped prompt a surge in the number of groups working on mechatronics. The trend has been fueled by falling prices for microprocessors and sensors, more stringent vehicle-emissions regulations in Europe and California, and automakers' wanting to enhance their vehicles with additional comfort and performance features.

Although the luxury market looms largest today—new high-end models from BMW contain more than 70 microprocessors that control more than 120 tiny motors—mechatronics will be moving into the wider car market within five years, says Lino Guzzella, codirector of the Institute of Measurement and Control at the Swiss Federal Institute of Technology. And with software like Isermann's on board, the electronic guts of these new driving machines should be as sturdy and reliable as steel. —*David Talbot*

IAN FOSTER & CARL KESSELMAN

Grid Computing

In the 1980s "internetworking protocols" allowed us to link any two computers, and a vast network of networks called the Internet exploded around the globe. In the 1990s the "hypertext transfer protocol" allowed us to link any two documents, and a vast, online library-cum-shopping-mall called the World Wide Web exploded across the Internet. Now, fast emerging "grid protocols" might allow us to link almost anything else: databases, simulation and visualization tools, even the number-crunching power of the computers themselves. And we might soon find ourselves in the midst of the biggest explosion yet.

"We're moving into a future in which the location of [computational] resources doesn't really matter," says Argonne National Laboratory's Ian Foster. Foster and Carl Kesselman of the University of Southern California's Information Sciences Institute pioneered this concept, which they call grid computing in analogy to the electric grid, and built a community to support it. Foster and Kesselman, along with Argonne's Steven Tuecke, have led development of the Globus Toolkit, an open-source implementation of grid protocols that has become the de facto standard. Such protocols promise to give home and office machines the ability to reach into cyberspace, find resources wherever they may be, and assemble them on the fly into whatever applications are needed.

Imagine, says Kesselman, that you're the head of an emergency response team that's trying to deal with a major chemical spill. "You'll probably want to know things like, What chemicals are involved? What's the weather forecast, and how will that affect the pattern of dispersal? What's the current traffic situation, and how will that affect the evacuation routes?" If you tried to find answers on today's Internet, says Kesselman, you'd get bogged down in arcane log-in procedures and incompatible software. But with grid computing it would be easy: the grid protocols provide standard mechanisms for discovering, accessing, and invoking just about any online resource, simultaneously building in all the requisite safeguards for security and authentication.

Construction is under way on dozens of distributed grid computers around the world—virtually all of them employing Globus Toolkit. They'll have unprecedented computing power and applications ranging from genetics to particle physics to earthquake engineering. The $88 million TeraGrid of the U.S. National Science Foundation will be one of the largest. When it's completed later this year, the general-purpose, distributed supercomputer will be capable of some 21 trillion floating-point operations per second, making it one of the fastest computational systems on Earth. And grid computing is experiencing an upsurge of support from industry heavyweights such as IBM, Sun Microsystems, and Microsoft.

OTHERS IN GRID COMPUTING

RESEARCHER	PROJECT
Andrew Chien Entropia	Peer-to-Peer Working Group
Andrew Grimshaw Avaki; U. Virginia	Commercial grid software
Miron Livny U. Wisconsin, Madison	Open-source system to harness idle workstations
Steven Tuecke Argonne National Laboratory	Globus Toolkit

IBM, which is a primary partner in the TeraGrid and several other grid projects, is beginning to market an enhanced commercial version of the Globus Toolkit.

Out of Foster and Kesselman's work on protocols and standards, which began in 1995, "this entire grid movement emerged," says Larry Smarr, director of the California Institute for Telecommunications and Information Technology. What's more, Smarr and others say, Foster and Kesselman have been instrumental in building a community around grid computing and in advocating its integration with two related approaches: peer-to-peer computing, which brings to bear the power of idle desktop computers on big problems in the manner made famous by SETI@home, and Web services, in which access to far-flung computational resources is provided through enhancements to the Web's hypertext protocol. By helping to merge these three powerful movements, Foster and Kesselman are bringing the grid revolution much closer to reality. And that could mean seamless and ubiquitous access to unfathomable computer power. —*M. Mitchell Waldrop*

UMAR MAHMOOD

Molecular Imaging

At Massachusetts General Hospital's Center for Molecular Imaging Research—a bustling facility nestled next to an old Navy shipyard—Umar Mahmood uses a digital camera to peer through the skin of a living mouse into a growing tumor. Using fluorescent tags and calibrated filters, the radiologist actually *sees* the effects of the cancer on a molecular scale: destructive enzymes secreted by the tumor show up on Mahmood's computer screen as splotches of red, yellow, and green. In the future, he says, such "molecular imaging" may lead to earlier detection of human disease, as well as more effective therapies.

Molecular imaging—shorthand for a number of techniques that let researchers watch genes, proteins, and other molecules at work in the body—has exploded, thanks to advances in cell biology, biochemical agents, and computer analysis. Research groups around the world are joining the effort to use magnetic, nuclear, and optical imaging techniques to study the molecular interactions that underlie biological processes. Unlike x-ray, ultrasound, and other conventional techniques that give doctors only such anatomical clues as the size of a tumor, molecular imaging could help track the underlying *causes* of disease. The appearance of an unusual protein in a cluster of cells, say, might signal the onset of cancer. Mahmood is helping to lead the effort to put the technology into medical practice.

It is challenging, though, to detect a particular molecule in the midst of cellular activity. When researchers inject a tag that binds to the molecule, they face the problem of distinguishing the bound tags from the extra, unbound tags. So Mahmood has worked with chemists to develop "smart probes" that change their brightness or their magnetic properties when they meet their target. "This is a big deal," says David Piwnica-Worms, director of the Molecular Imaging Center at Washington University in St. Louis. The method, he explains, "allows you to see selected proteins and enzymes that you might miss with standard tracer techniques."

In a series of groundbreaking experiments, Mahmood's team treated cancerous mice with a drug meant to block the production of an enzyme that promotes tumor growth. The researchers then injected fluorescent probes designed to light up in the presence of that enzyme. Under an optical scanner, treated tumors showed up as less fluorescent than untreated tumors, demonstrating the potential of molecular imaging to monitor treatments in real time—rather than waiting months to see whether a tumor shrinks. "The big goal is to select the optimum therapy for a patient and then to check that, say, a drug is hitting a particular receptor," says John Hoffman, director of the Molecular Imaging Program at the National Cancer Institute. What's more, molecular imaging could be used to detect cancer signals that precede anatomical changes by months or years, eliminating the need for surgeons to cut out a piece of tissue to make a diagnosis. "At the end of the day, we may replace a number of biopsies with imaging," Mahmood says.

In Mahmood's lab, clinical trials are under way for magnetic resonance imaging of blood vessel growth—an early indicator of tumor growth and other changes. For more advanced techniques such as those used in the mouse cancer study, clinical trials are two years away. The big picture: 10 years down the road, molecular imaging may take the place of mammograms, biopsies, and other diagnostic techniques. Although it won't replace conventional imaging entirely, says Mahmood, molecular imaging will have a profound effect both on basic medical research and on high-end patient care. Indeed, as his work next door to the shipyard makes clear, an important new field of biotechnology has set sail. —*Gregory T. Huang*

OTHERS IN
MOLECULAR IMAGING

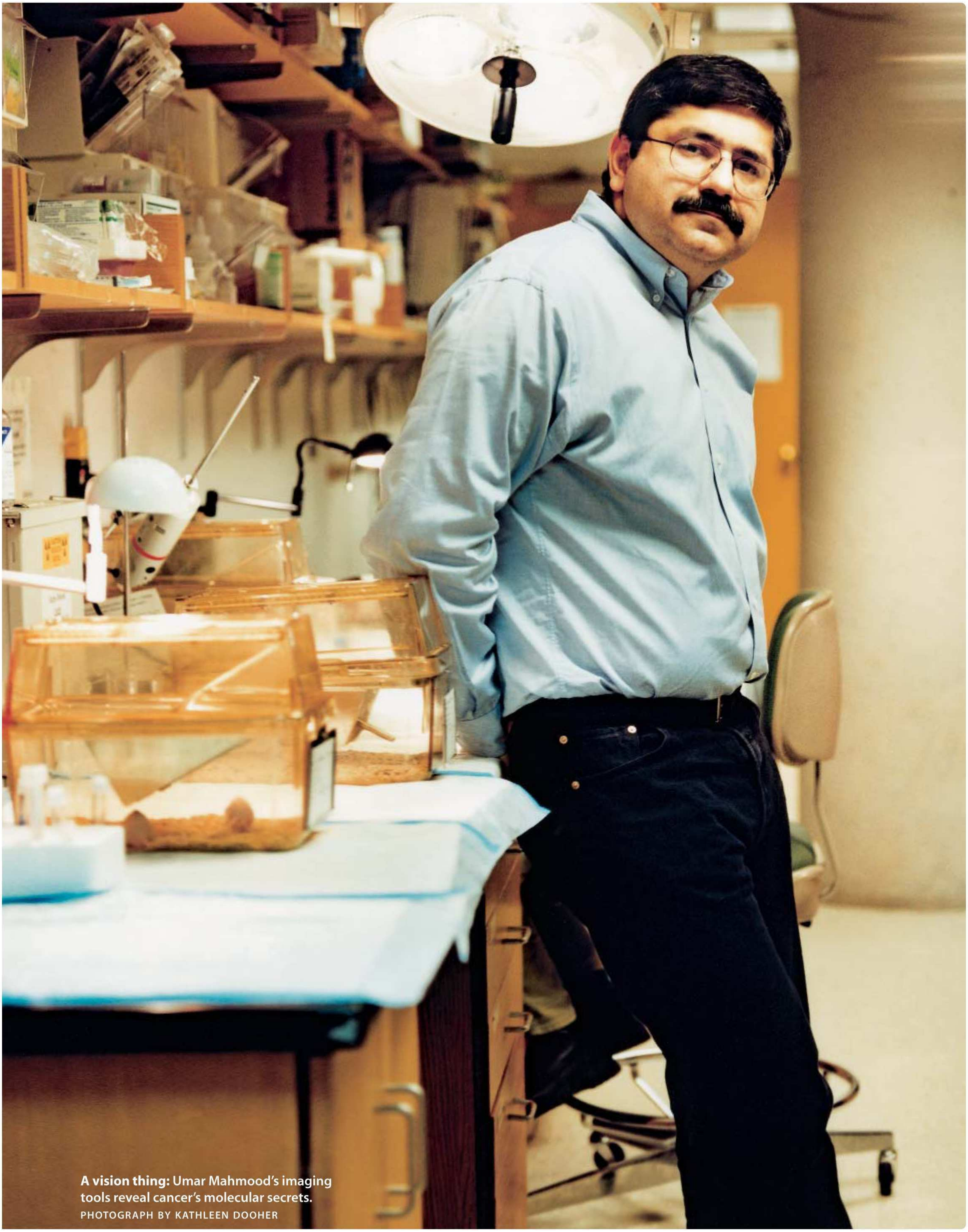
RESEARCHER	PROJECT
Ronald Blasberg Memorial Sloan-Kettering Cancer Center	Imaging of gene expression
Harvey Herschman U. California, Los Angeles	Tracking of gene therapy, gene activities
David Piwnica-Worms Washington U.	Protein interactions, imaging tools
Patricia Price U. Manchester	Clinical oncology, imaging drug targets
Ralph Weissleder Harvard Medical School	Cell tracking, molecular targets, drug discovery

STEPHEN CHOU

Nanoimprint Lithography

A world of Lilliputian sensors, transistors, and lasers is in development at nanotechnology labs worldwide. These devices point to a future of ultrafast and cheap electronics and communications. But making nanotechnology relevant beyond the lab is difficult because of the lack of suitable manufacturing techniques. The tools used to mass-produce silicon microchips are far too blunt for nanofabrication, and specialized lab methods are far too expensive and time-consuming to be practical. "Right now everybody is talking about nanotechnology, but the commercialization of nanotechnology critically depends upon our ability to manufacture," says Princeton University electrical engineer Stephen Chou.

A mechanism just slightly more sophisticated than a printing press could be the answer, Chou believes. Simply by stamping a hard mold into a soft material, he can faithfully imprint features smaller



A vision thing: Umar Mahmood's imaging tools reveal cancer's molecular secrets.
PHOTOGRAPH BY KATHLEEN DOOHER

than 10 nanometers across. Last summer, in a dramatic demonstration of the potential of the technique, Chou showed that he could make nano features directly in silicon and metal. By flashing the solid with a powerful laser, he melted the surface just long enough to press in the mold and imprint the desired features.

Although Chou was not the first researcher to employ the imprinting technique, which some call soft lithography, his demonstrations have set the bar for nanofabrication, says John Rogers, a chemist at Lucent Technologies' Bell Labs. "The kind of revolution that he has achieved is quite remarkable in terms of speed, area of patterning, and the smallest-size features that are possible. It's leading edge," says Rogers. Ultimately, nanoimprinting could become the method of choice for cheap and easy fabrication of nano features in such products as optical components for communications and gene chips for diagnostic screening. Indeed, NanoOpto, Chou's startup in Somerset, NJ, is already shipping nanoimprinted optical-networking components. And Chou has fashioned gene chips that rely on nano channels imprinted in glass to straighten flowing DNA molecules, thereby speeding genetic tests.

Chou is also working to show that nanoimprinting can tackle lithography's grand challenge: how to etch nano patterns into silicon for future generations of high-performance microchips. Chou says he can already squeeze at least 36 times as many transistors onto a silicon wafer as the most advanced commercial lithography tools. But to make complex chips, which have many layers, perfect alignment must be maintained through as many as 30 stamping steps. For Chou's process, in which heat could distort the mold and the wafer, that means each round of heating and imprinting must be quick. With his recent laser-heating innovations, Chou has cut imprinting time from 10 seconds to less than a microsecond. As a result, he has demonstrated the ability to make basic multilayered chips, and he says complex processors and memory chips are next. Chou's other startup, Nanonex in Princeton, NJ, is busy negotiating alliances with lithography tool manufacturers.

Chou's results come at a time when the chipmaking industry has been spending billions of dollars developing exotic fabrication techniques that use everything from extreme ultraviolet light to electron beams. But, says Stanford University nanofabrication expert R. Fabian Pease, "If you look at what the extreme ultraviolet and the electron projection lithography techniques have actually accomplished, [imprint lithography], which has had a tiny fraction of the investment, is looking awfully good." This is sweet vindication for Chou, who began working on nanofabrication in the 1980s, before most of his colleagues recognized that nano devices would be worth manufacturing. "Nobody questions the manufacturing ability of nanoimprint anymore," says Chou. "Suddenly the doubt is gone." —*Peter Fairley*

OTHERS IN
NANOIMPRINT LITHOGRAPHY

RESEARCHER	PROJECT
Yong Chen Hewlett-Packard	High-density molecular electronic memory
John Rogers Bell Labs	Patterning polymer electronics
George Whitesides Harvard U.	Contact printing on flexible substrates
Grant Willson U. Texas; Molecular Imprints	High-density microchip fabrication

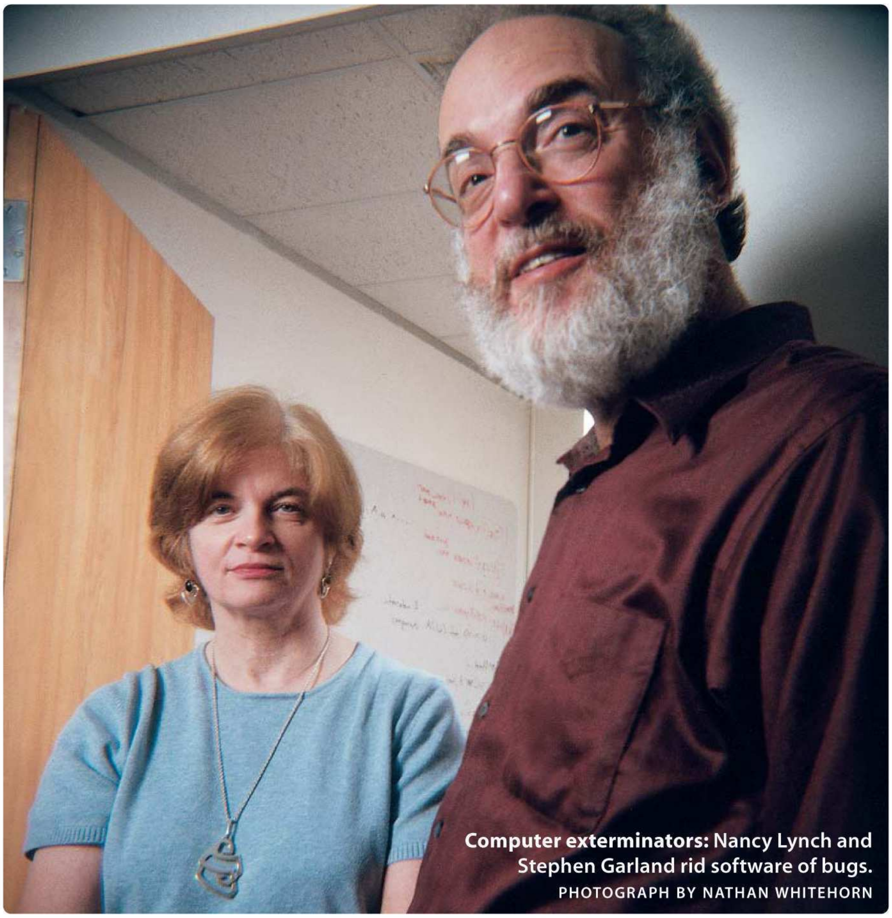
Nano's Gutenberg: With the ease of a printing press, Stephen Chou makes tiny devices.
PHOTOGRAPH BY FLYNN LARSEN

NANCY LYNCH & STEPHEN GARLAND

Software Assurance

Computers crash. That's a fact of life. And when they do, it's usually because of a software bug. Generally, the consequences are minimal—a muttered curse and a reboot. But when the software is running complex distributed systems such as those that support air traffic control or medical equipment, a bug can be very expensive, and even cost lives. To help avoid such disasters, Nancy Lynch and Stephen Garland are creating tools they hope will yield nearly error-free software.

Working together at MIT's Laboratory for Computer Science, Lynch and Garland have developed a computer language and programming tools for making software development more rigorous, or as Garland puts it, to "make software engineering more like an engineering discipline." Civil engineers, Lynch points out, build and test a model of a bridge before anyone constructs the bridge itself. Programmers,



Computer exterminators: Nancy Lynch and Stephen Garland rid software of bugs.
PHOTOGRAPH BY NATHAN WHITEHORN

however, often start with a goal and, perhaps after some discussion, simply sit down to write the software code. Lynch and Garland's tools allow programmers to model, test, and reason about software before they write it. It's an approach that's unique among efforts launched recently by the likes of Microsoft, IBM, and Sun Microsystems to improve software quality and even to simplify and improve the programming process itself.

Like many of these other efforts, Lynch and Garland's approach starts with a concept called abstraction. The idea is to begin with a high-level summary of the goals of the program and then write a series of progressively more specific statements that describe both steps the program can take to reach its goals and how it should perform those steps. For example, a high-level abstraction for an aircraft collision avoidance system might specify that corrective action take place whenever two planes are flying too close. A lower-level design might have the aircraft exchange messages to determine which should ascend and which should descend.

Lynch and Garland have taken the idea of abstraction further. A dozen years ago, Lynch developed a mathematical model that made it easier for programmers to tell if a set of abstractions would make a distributed system behave correctly. With this model, she and Garland created a computer language programmers can use to write "pseudocode" that describes what a program should do. With his students, Garland has also built tools to prove that lower levels of abstractions relate correctly to higher levels and to simulate a program's behavior before it is translated into an actual programming language like Java. By directing programmers' attention to many more possible bug-revealing circumstances than might be checked in typical software tests, the tools help assure that the software will always work properly. Once software has been thus tested, a human can easily translate the pseudocode into a standard programming language.

Not all computer scientists agree that it is possible to prove software error free. Still, says Shari Pfleeger, a computer scientist for Rand in Washington, DC, mathematical methods like Lynch and Garland's have a place in software design. "Certainly using it for the most critical parts of a large system would be important, whether or not you believe you're getting 100 percent of the problems out," Pfleeger says.

While some groups have started working with Lynch and Garland's software, the duo is pursuing a system for automatically generating Java programs from highly specified pseudocode. The aim, says Garland, is to "cut human interaction to near zero" and eliminate transcription errors. Collaborator Alex Shvartsman, a University of Connecticut computer scientist, says, "A tool like this will take us slowly but surely to a place where systems are much more dependable than they are today." And whether we're boarding planes or going to the hospital, we can all appreciate that goal. —*Erika Jonietz*

OTHERS IN
SOFTWARE ASSURANCE

RESEARCHER	PROJECT
Gerard Holzmann Bell Labs	Software to detect bugs in networked computers
Charles Howell Mitre	Benchmarks for software assurance
Charles Simonyi Intentional Software	Programming tools to improve software
Douglas Smith Kestrel Institute	Mechanized software development

JAMES PAULSON

Glycomics

James Paulson, a researcher at the Scripps Research Institute in La Jolla, CA, lifts a one-liter, orange-capped bottle from his desk. The bottle is filled with sugar, and Paulson estimates that, had the substance been purchased from a chemical supply house, it would have cost about $15 million. "If I could only sell it," Paulson jokes, admiring what looks like the chunky, raw sugar served at health food restaurants.

In fact, Cytel, a biotech company Paulson once helped run, synthesized the sugar—one of thousands made by the human body—with hopes it could be sold to truly boost health. Cytel's aim was to turn the sugar into a drug that could tame the immune system to minimize damage following heart attacks and surgery. That ambition failed, but the effort to understand and ultimately harness sugars—a field called glycomics—is thriving. And Paulson, who has gone on to cofound Abaron Biosciences in La Jolla, CA, is leading the way, developing new glycomic

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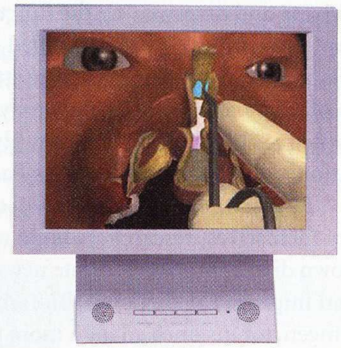

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The Smile Train is an international charity dedicated to helping children with cleft lips and palates.

This year, The Smile Train will provide free cleft surgery for more than 25,000 desperately poor children who have no place else to turn. In as little as 45 minutes and for just $250, The Smile Train can give a child not just a new smile, but a second chance at life.

What makes The Smile Train unique is that every surgery it provides is performed by local doctors in developing countries. By using virtual surgery software, The Smile Train is able to provide free, high-quality training for doctors half a world away. This software will produce better cleft surgeons in a fraction of the time it used to take.

Visit www.SmileTrain.org to find out more. And if you want to help them change the world one smile at a time, make a donation, and we'll match it 100%.

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drugs that could have an impact on health problems ranging from rheumatoid arthritis to the spread of cancer cells.

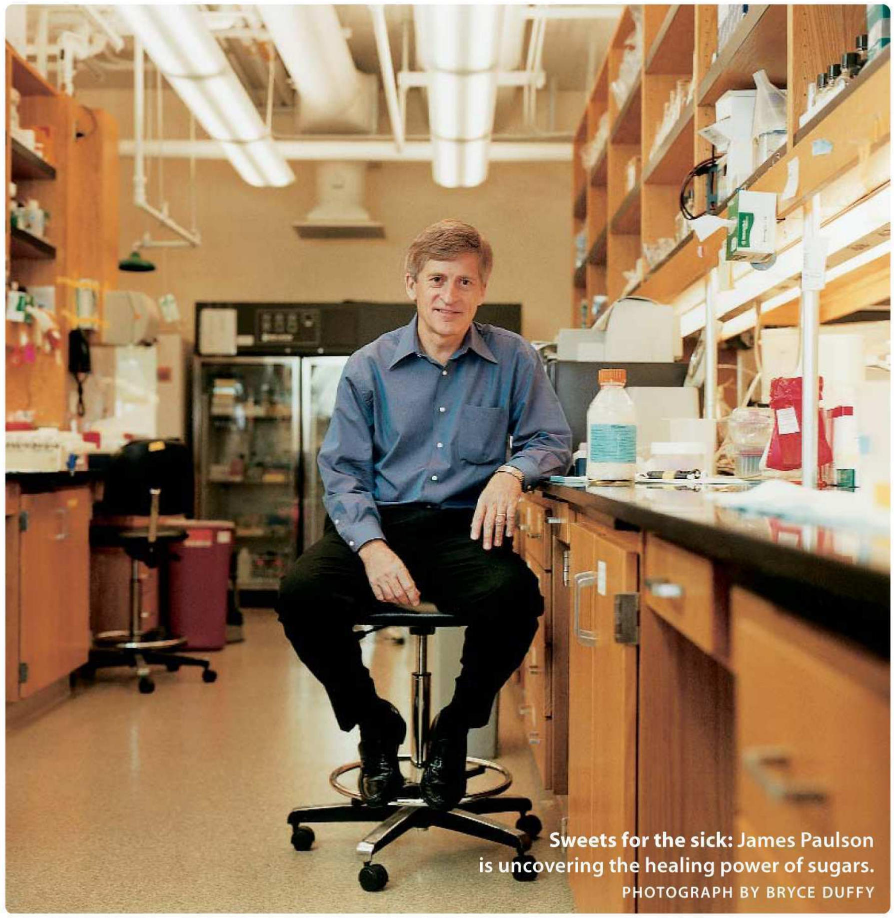
The reason for the excitement around glycomics is that sugars have a vital, albeit often overlooked, function in the body. In particular, sugars play a critical role in stabilizing and determining the function of proteins through a process called glycosylation, in which sugar units are attached to other molecules including newly made proteins. "If you don't have any glycosylation, you don't have life," says Paulson.

By manipulating glycosylation or sugars themselves, researchers hope to shut down disease processes, create new drugs, and improve existing ones. Biotech giant Amgen, for instance, made a more potent version of its best-selling drug (a protein called erythropoietin, which boosts red-blood-cell production) by attaching two extra sugars to the molecule. Other companies such as GlycoGenesys, Progenics Pharmaceuticals, and Oxford Glycoscience have glycomic drugs in human tests for ailments ranging from Gaucher's disease to colorectal cancer. "The medical potential...is absolutely enormous," says Abaron cofounder Jamey Marth, a geneticist at the University of California, San Diego.

Despite the importance of sugars, efforts to unravel their secrets long remained in the shadows of research into genes and proteins—in part because there is no simple "code" that determines sugars' structures. But over the last few decades, researchers have slowly uncovered clues to sugars' functions. In the late 1980s, Paulson and his team isolated a gene for one of the enzymes responsible for glycosylation. Since that watershed event, scientists have been piecing together an ever more detailed understanding of the ways sugars can in some instances ensure healthy functioning and in others make us susceptible to disease.

It's a gargantuan task. Researchers estimate that as many as 40,000 genes make up each person, and each gene can code for several proteins. Sugars modify many of those proteins, and various cell types attach the same sugars in different ways, forming a variety of branching structures, each with a unique function. "It's a nightmare" to figure all this out, says Paulson. "In order for the field to progress rapidly, we need to bring together the experts in the various subfields to think about the problems of bridging the technologies and beginning to move toward a true glycomics approach." In an attempt do just that, Paulson heads the Consortium for Functional Glycomics. The group, comprising more than 40 academics from a number of disciplines, has a five-year $34 million grant from the National Institutes of Health.

Despite this large-scale effort and healthy dose of federal funding, however, Paulson stresses that the consortium cannot detail every sugar in the body. "We're just taking a bite out of the apple." But what a sweet, large apple it is. —*Jon Cohen*



Sweets for the sick: James Paulson is uncovering the healing power of sugars.
PHOTOGRAPH BY BRYCE DUFFY

OTHERS IN GLYCOMICS

RESEARCHER	PROJECT
Carolyn Bertozzi U. California, Berkeley; Thios Pharmaceuticals	Glycosylation and receptor binding in disease
Richard Cummings U. Oklahoma	Sugars in cell adhesion
Stuart Kornfeld Washington U. School of Medicine	Pathways of glycosylation and genetic disorders
John Lowe U. Michigan	Sugars in immunity and cancer
Jamey Marth U. California, San Diego; Abaron Biosciences	Sugars in physiology and disease

NICOLAS GISIN

Quantum Cryptography

The world runs on secrets. Governments, corporations, and individuals—to say nothing of Internet-based businesses—could scarcely function without secrecy. Nicolas Gisin of the University of Geneva is in the vanguard of a technological movement that could fortify the security of electronic communications. Gisin's tool, called quantum cryptography, can transmit information in such a way that any effort to eavesdrop will be detectable.

The technology relies on quantum physics, which applies at atomic dimensions: any attempt to observe a quantum system inevitably alters it. After a decade of lab experiments, quantum cryptography is approaching feasibility. "We can now think about using it for practical purposes," says Richard Hughes, a quantum cryptography pioneer at the Los Alamos National Laboratory in New Mexico. Gisin—a physicist and entre-

preneur—is leading the charge to bring the technology to market.

The company that Gisin spun off from his University of Geneva laboratory in 2001, id Quantique, makes the first commercially available quantum-cryptography system, he says. The PC-size prototype system includes a random-number generator (essential for creating a decryption key) and devices that emit and detect the individual photons of light that make up the quantum signal.

Conventional cryptographers concentrate on developing strong digital locks to keep information from falling into the wrong hands. But even the strongest lock is useless if someone steals the key. With quantum cryptography, "you can be certain that the key is secure," says Nabil Amer, manager of the physics of information group at IBM Research. Key transmission takes the form of photons whose direction of polarization varies randomly. The sender and the intended recipient compare polarizations, photon by photon. Any attempt to tap this signal alters the polarizations in a way that the sender and intended recipient can detect. They then transmit new keys until one gets through without disturbance.

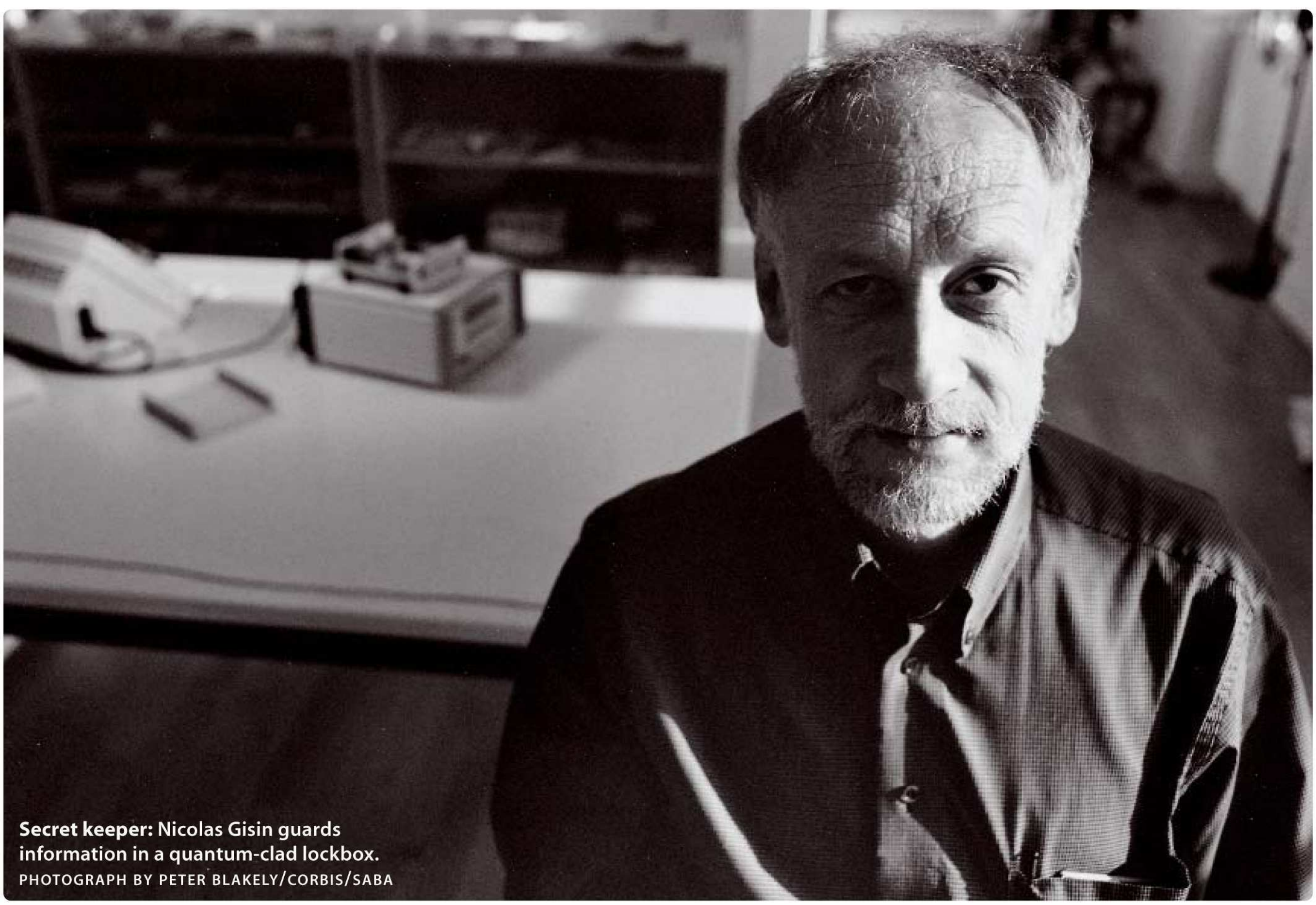
Quantum cryptography is still ahead of its time. Nonquantum encryption schemes such as the public-key systems now commonly used in business have yet to be cracked. But the security of public-key systems relies on the inability of today's computers to work fast enough to break the code. Ultimately, as computers get faster, this defense will wear thin. Public-key encryption, Gisin says, "may be good enough today, but someone, someday, will find a way to crack it. Only through quantum cryptography is there a guarantee that the coded messages sent today will remain secret forever."

Gisin has no illusions about the challenges he faces. For one thing, quantum cryptography works only over the distance a light pulse can travel through the air or an optical fiber without a boost; the process of amplification destroys the quantum-encoded information. Gisin's team holds the world's distance record, having transmitted a quantum key over a 67-kilometer length of fiber connecting Geneva and Lausanne, Switzerland.

The work of Gisin and others could usher in a new epoch of quantum information technology. Ironically, it is in part the prospect that superfast quantum computers will someday supply fantastic code-breaking power that drives Gisin and others to perfect their method of sheltering secret information. In the coming decades, Gisin contends, "e-commerce and e-government will be possible only if quantum communication widely exists." Much of the technological future, in other words, depends on the science of secrecy. —*Herb Brody*

OTHERS IN QUANTUM CRYPTOGRAPHY

RESEARCHER	PROJECT
Nabil Amer IBM	Quantum key exchange through optical fiber
Richard Hughes Los Alamos National Laboratory	Ground-to-satellite optical communications
John Preskill Caltech	Quantum information theory
John Rarity QinetiQ	Through-air quantum-key transmission
Alexei Trifonov and Hoi-Kwong Lo MagiQ Technologies	Quantum-cryptography hardware



Secret keeper: Nicolas Gisin guards information in a quantum-clad lockbox.
PHOTOGRAPH BY PETER BLAKELY/CORBIS/SABA

call for nominations

THE YOUNG INNOVATORS WHO WILL CREATE THE FUTURE

TR100

TR100/2003

What will the world look like 5, 10, 30 years down the road? Who are the leading young innovators already laying the foundation for this technological future? Help us find them and tell their stories. Nominations are now open for the 2003 edition of the TR100, *Technology Review*'s list of 100 young people whose contributions to emerging technologies will profoundly influence our world. Nominees should not turn 35 before January 1, 2003, and their work should exemplify the spirit of innovation. *Technology Review* will profile all 100 in a special October 2003 issue and recognize them at an awards celebration.

Anyone can nominate candidates, including himself or herself, by using the simple online form at www.technologyreview.com/tr100/nomination/.

The deadline for submissions is February 1, 2003.

AN MIT ENTERPRISE
TECHNOLOGY
REVIEW

supercomputing resurrected

Japan's Earth Simulator puts other fast supercomputers to shame. Shocked at falling behind, U.S. computer maestros are cooking up radical ways to build these powerful beasts.

By Claire Tristram

Better, faster, costlier: The $350 million Earth Simulator outpaces the next five speediest supercomputers combined.
PHOTOGRAPH BY TOM WAGNER/CORBIS/SABA

Even in a field defined by continuous breakthroughs, the achievement was a shocker: last March the Japanese government fired up a computer that soon proved to be the fastest in the world, in some cases outperforming the next-fastest computer by a factor of 10. The Earth Simulator, built by NEC, took four years to assemble and cost at least $350 million. It quickly delivered real-world scientific results in global-climate modeling, completing simulations that made other computers look crude. Scientists worldwide lined up for the limited amount of computer time available to researchers outside Japan. By June, just weeks after the machine hummed to life, three of the six finalists for the prestigious Gordon Bell awards in high-performance computing had run their projects on the Earth Simulator.

A smattering of articles last spring covered the news, quoting experts who compared the Earth Simulator to Sputnik—another instance of the United States' having been severely outclassed in a critical technology. But outside the rarefied circles of high-end computing, the story soon died. U.S. computer vendors have been downplaying the achievement, dismissing the Earth Simulator as "old technology" or "too specialized" to be of much use, even insisting that it was a "publicity stunt." "Give us $400 million to spend on a single computer, and we could build something just as fast," says Peter Ungaro, vice president of high-performance computing at IBM.

"I love that," scoffs Gordon Bell, designer of the first minicomputer for Digital Equipment and a luminary in high-performance computing. "How is IBM going to do it? Where is the technology? I want to bet $1,000 that in the next year, IBM can't match the cost performance of the Earth Simulator on any system they have." In fact, IBM recently won a Department of Energy contract to build a pair of machines designed to run at two to nine times the speed of the Earth Simulator, but the project will take until 2005 to complete. Like many of those involved in high-powered scientific computing, Bell believes that Japan's achievement has exposed a gaping hole in the development of supercomputer systems in the United States—a hole that money alone can't fill.

What happened that allowed NEC to take such a tremendous lead in computing power? Simply put, the Japanese government saw fit to subsidize the development of the world's most expensive computer. The project's goal was not to grab bragging rights from the United States, but to advance scientists' understanding of the global climate by creating a machine that performs better modeling and weather simulations than ever before.

At the same time, U.S. government funding for research on high-end computing was waning in response to the deeply felt U.S. notion that supercomputer developers—like welfare moms—should take care of themselves rather than survive on government handouts. Compared with any other part of the computer market, the market for supercomputers is small and slow growing, so when public funding dried up, private investment in high-performance architectures dried up too. For the past decade or so, the U.S. emphasis in supercomputing has therefore been on linking clusters of commodity processors—those designed for everyday business applications—in what are known as massively parallel configurations. That approach is a stark contrast to the Japanese vision of specialized architectures developed solely for the high-performance market.

Granted, the commodity approach has gone far: at this writing two commodity machines, the twin Hewlett-Packard-built ASCI Q supercomputers at Los Alamos National Laboratory in New Mexico, rank as second-fastest in the world (as measured by Top500.org, a nonprofit analysis group). The idea of harnessing many low-end processors to do complicated tasks has captured the public imagination as well, with projects such as SETI@home, which enlists the desktop computers of more than four million volunteers to scan radio telescope data for patterns indicative of alien intelligence. Beowulf clusters, which use a method developed in 1994 for linking PCs together to maximize their processing power, have made it even easier to reach high-performance levels with relatively low capital investment. Without question, the commodity approach has proved itself for many applications that at one time ran on specialized "big iron."

But in spite of these gains, the United States has fallen painfully short in the very field where computing muscle matters most and where the nation has the most to gain: in simulating such complex systems as weather on the macroscopic end and protein folding on the microscopic. This simulation capability is increasingly vital for the advancement of basic science, as well as for national security.

Making the private sector pay for this capability is "like the defense industry's saying nuclear submarines have to have some sort of commercial spinoff," says Horst Simon, director of the National Energy Research Scientific Computing Center in Oakland, CA, home to the 12th-fastest computer. "We've embarked on a direction in the United States that is not going to work."

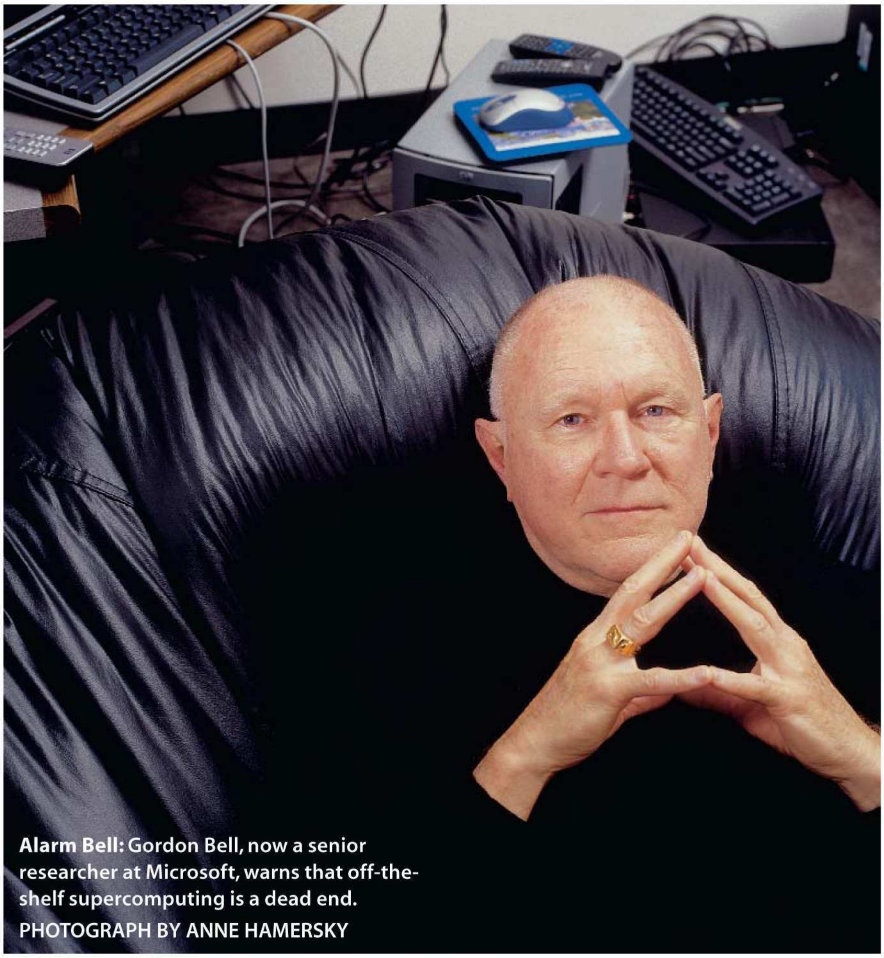
The Need for Speed

What are the real advantages of making computers ever faster? Why, after all, can't we use a machine that takes a month or a

Who Makes the Most Superfast Computers?

COMPANY	NUMBER IN TOP 500	SPECIFICATIONS OF FASTEST MACHINE NAME	 SPEED (GIGAFLOPS)	 LOCATION
Hewlett-Packard	137	ASCI Q	7,727	Los Alamos National Laboratory, NM
IBM	129	ASCI White	7,226	Lawrence Livermore National Laboratory, CA
Sun Microsystems	88	HPC 4500	420	Swedish Armed Forces, Stockholm, Sweden
Silicon Graphics	45	ASCI Blue Mountain	1,608	Los Alamos National Laboratory, NM
Cray	22	T3E 1200	1,166	Unknown (U.S. government)
NEC	15	Earth Simulator	35,860	Earth Simulator Center, Yokohama, Japan

SOURCE: TOP500.ORG



Alarm Bell: Gordon Bell, now a senior researcher at Microsoft, warns that off-the-shelf supercomputing is a dead end.
PHOTOGRAPH BY ANNE HAMERSKY

week to complete a task instead of a day or an hour? For many problems, we can. But the truth is, we're just beginning to gain the computing power to understand what is going on in systems with thousands or millions of variables; even the fastest machines are just now revealing the promise of what's to come.

Take, for instance, greenhouse gases and the way they affect the global climate, one of the problems the Earth Simulator was built to study. With computers fast enough to predict climate changes accurately, we can know with far greater certainty what level of atmospheric carbon dioxide will melt the polar ice caps. Similarly, because the Earth Simulator models the planet's climate at an incredible degree of granularity, it can carry out simulations that account for the effects of such local phenomena as thunderstorms. These phenomena may affect areas only 10 kilometers wide—in contrast to the 30 to 50 kilometers most weather models use as the standard grid size.

Or take the difficulties we've encountered trying to understand and harness nuclear fusion—that perpetually just-out-of-reach panacea for our energy problems. "It can take a decade to perform a single [fusion] experiment," says Thomas Sterling, faculty associate at the Center for Advanced Computing Research at Caltech. "Faster computers would accelerate these projects by decades, allowing us not only to design safe reactors that give us the power to run the planet, but also to know how to get rid of the waste."

One recent example of both the promise and the limitations of today's most powerful computers came from IBM's ASCI White machine, the world's fourth-fastest supercomputer, which IBM researchers used to investigate how materials crack and deform under stress. The study, announced last spring, simulated the behavior of a billion copper atoms. A billion certainly sounds like a lot of variables—until you realize that it would take more than a hundred trillion times that number of atoms to make up even a cubic centimeter of copper.

"There's a notion out there that high-performance computing is a mature industry, where all the problems have been solved, and we've moved on," says Burton Smith, chief scientist at Cray, a pioneering supercomputer company in Seattle. "That is false. The embarrassment of the Earth Simulator reveals the fact that there is still plenty more understanding to be had."

Custom versus Commodity

Over the last decade, everything we've heard about computers has been about making them smaller, faster, cheaper, more like commodities. Our laptops, for instance, have the same capabilities as a Cray computer from the mid-1970s. Then along comes the monstrous Earth Simulator: it's the size of four tennis courts, and it cost almost twice as much as its closest competition, the ASCI Q machines. If this is the future of supercomputing, what are we to make of it? The machine doesn't even boast a particularly new architecture: NEC used a technique called vector computing, which dates from Cray's earliest days.

But beyond its ungainliness and architectural oddities, the Earth Simulator exemplifies an approach to high-performance computing that is fundamentally different from the one followed by most U.S. computer makers today. The Earth Simulator was designed from the bottom up—from its processors to the communications buses that link processors and memory—to be the world's fastest computer. When will the U.S. approach of linking general-purpose processors like those that serve up Web pages produce a result that can match the performance of a machine explicitly designed for performance? "My view is that you can't do it," says Bell. "I simply don't see a way, with a general-purpose computer, of getting from there to here."

The performance challenge begins with the processor. The data crunched in scientific computation often take the shape of lists of numbers, the values associated with real-world observations. Traditionally, computers acted on these values sequentially, retrieving them from memory one by one. Then, in the early 1970s, Seymour Cray took an intuitive leap: why not design a computer so that its processors can request an entire list, or "vector," all at once, rather than waiting for memory to respond to each request in turn? Such a processor would spend more time computing and less time waiting for data from memory. From the mid-1970s through the 1980s, Cray's vector supercomputers set record after record. But they required expensive specialized chips, and vector computing was, therefore, largely abandoned in the United States after 1990, when the notion of massively parallel systems made from off-the-shelf processors took hold.

THERE'S NOT ENOUGH ART IN OUR SCHOOLS.

NO WONDER PEOPLE SAY "GESUNDHEIT" WHEN YOU SAY

"TCHAIKOVSKY."

If one were to make a quick list of the world's favorite composers, despite his relatively recent vintage Peter Ilyich Tchaikovsky would be on it. After all, he did compose *Swan Lake*, which is perhaps the most famous ballet of all time. And there can't be more than just a handful of ballet companies that don't perform *The Nutcracker* every Christmas.

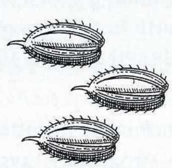


Fig. 1 Pollen

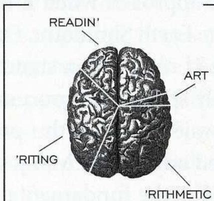
Causes watery eyes. Much like Tchaikovsky's composition "Romeo and Juliet."

Peter Ilyich Tchaikovsky endured many setbacks, not the least of which was a blind barber.

Indeed, this great Romantic composer should be so immortalized. As a young man, he pursued a career in music at enormous personal risk and against his own father's advice. His mild temperament combined with his tendency to work too hard left him with insomnia, debilitating headaches and hallucinations. On top of that, Tchaikovsky's composition teacher never liked his work, even after he became world-famous.

Setbacks like these could have finished a lesser man. Instead, they informed his work, which remains some of the best loved in history. Yet some kids will still confuse Tchaikovsky with a nasal spasm.

Why? Because the arts are slowly but surely being eliminated from today's schools, even though a majority of the parents believe music and drama and dance and art make their children better students and better people.



Someone isn't getting their recommended daily allowance of art.

To help reverse this disturbing trend, or for more information about all the many benefits of arts education, visit us at AmericansForTheArts.org. Or else Tchaikovsky could seem like just another casualty of allergy season.

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AMERICANS for the ARTS

DORIS DUKE CHARITABLE FOUNDATION

White-hot secrets: Classified-weapons simulation is one priority for ASCI White, the world's fourth-fastest supercomputer.
PHOTOGRAPH BY ANNE HAMERSKY

Vector computing nevertheless remained one of the most efficient ways to handle large-scale simulations, prompting NEC to adopt Cray's approach when it bid for the government contract to build the Earth Simulator. Once NEC's architects decided to build for speed rather than standardization, they were free to develop not only specialized processors, but also wider communications pathways between the processors, compounding the hardware's speed advantage. Many such improvements are built into the NEC SX6, the fundamental building block of the Earth Simulator. "Vector architecture is the best fit for computer simulations of 'grand challenge' scientific and engineering problems such as global warming, supersonic-airplane design, and nanoscale physics," says Makoto Tsukakoshi, a general manager for the Earth Simulator project at NEC.

Yoking together commodity machines with standard commercial networks, on the other hand, shifts the speed burden from hardware to software. Computer scientists must write "parallel programs" that parse problems into chunks, then explicitly control which processors should handle each chunk—all in an effort to minimize the time spent passing bits through communications bottlenecks between processors.

Such programming has proved extremely difficult: a straightforward FORTRAN program becomes a noodly mess of code that calls for rewriting and debugging by parallel-programming specialists. "I hope to concentrate my attention on my research rather than on how to program," says Hitoshi Sakagami, a researcher at Japan's Himeji Institute of Technology and a Gordon Bell Prize finalist for work using the Earth Simulator. "I don't consider parallel computers acceptable tools for my research if I'm constantly forced to code parallel programs."

It's not laziness that has kept programmers from finding better ways to write parallel code. "People have worked extremely hard trying to develop new application software based on different algorithms to use parallel machines, with little success," says Jim Decker, principle deputy director of the Office of Science in the Department of Energy. (Decker's agency is responsible for basic research in areas such as energy and the environment.) Vector machines often employ their own form of parallel processing, but the mathematics for doing so is far less complicated; Earth Simulator scientists, for example, are able to program using a flavor of the classic FORTRAN computer language that takes a much more direct approach.

A supercomputer comprising large numbers of commercial processors isn't just hard to program. It has become clear that the gains from adding more processors to a commodity system eventually flatten into insignificance as coaxing them to work together grows more difficult. What really got computational scientists' hearts racing about the Earth Simulator was not the

peak—or maximum number of calculations performed per second—which is roughly four times the capacity of the next fastest machine and in itself is impressive enough. Instead, it was the computer's capability for real problem solving (which, after all, is what scientists care about). The Earth Simulator can crunch computations at up to 67 percent of its peak capacity over a sustained period. In comparison, the massively parallel approach—well, it doesn't compare.

"If you throw enough of these commodity processors into a system, and you're not overwhelmed by the cost of the communications network to link them together, then you might eventually reach the peak performance of the Earth Simulator," says Sterling. "But what is rarely reported publicly about these systems is that their sustained performance is frequently below five percent of peak, or even one percent of peak."

Although it's certainly cheaper to build supercomputers out of commodity parts, many computational scientists suspect that the cost of developing parallel software actually makes it more expensive to run scientific applications on such a machine.

"People have gotten enamored of the low cost for what sounds like a very high level of performance on commodity machines," says Decker. "But they aren't really cheaper to build. We need to look at sustained performance, as well as the cost of developing software. Software costs are generally larger than hardware costs, so if there are hardware approaches that make it easy to solve the problem, we're better off investing in hardware. In hindsight, I believe we would have been better off taking a different path."

Playing Catch-Up

If the Earth Simulator really were viewed as another Sputnik, right about now the U.S. government would be budgeting some serious cash for supercomputing research and development. After all, NASA spent more than $19 billion—roughly $80 billion in today's dollars—on the Apollo missions to put a man on the moon. But George W. Bush is no John F. Kennedy, and the race to overtake the Earth Simulator has captured neither the public's imagination nor a corresponding level of public funding.

There is, however, one recurring driver for U.S. spending on supercomputing—the need for more computational power to simulate nuclear weapons performance in place of underground testing. In November the Energy Department's National Nuclear Security Administration awarded IBM a three-year, $267 million contract to build two supercomputers—ASCI Purple and Blue Gene/L—which are projected to have more combined processing power than today's 500 fastest supercomputers put together. And in response to the Earth Simulator, the U.S. Defense Advanced Research Projects Agency has begun its own, more modest program to fund supercomputer research. The agency is starting with individual $3 million research grants to industry leaders Cray, IBM, Hewlett-Packard, Silicon Graphics, and Sun Microsystems, to be followed by additional funds if technology milestones are met. The new defense projects have begun to reenergize the industry. Cray's Burton Smith says, "This really marks the end of a fairly long period where the government hasn't been involved in computer research and development."

Another way to jump-start U.S. supercomputing might be through additional investment in vector computing, an approach the Earth Simulator proves was prematurely abandoned by U.S. developers. "The current state of high-performance architecture goes back to the robustness of the 25-year-old basic Cray vector architecture that NEC adopted and continues to improve," says Bell. "United States architects have rejected the architecture while failing to develop competitive alternatives."

But where will new vector computers be developed? Just as the United States once fell behind in consumer electronics, it also rapidly lost the expertise needed to build such systems. Out of the 40-odd companies that specialized in high-performance computing in the late 1980s, only Cray remains in business, having survived acquisition by Silicon Graphics in 1996 and Tera in 2000. (Tera promptly changed its own name to Cray in acknowledgment of the company's singular prominence in the field.) Cray is the only U.S. supercomputer maker to support vector processing. Last fall Cray started shipping a new vector computer, the X1; fully loaded, the machine will outpace the Earth Simulator by almost 50 percent, the company says. But Cray has not yet sold an X1 system that powerful, and while the U.S. Army and the Department of Energy are evaluating its potential, other customers are understandably wary of depending on an architecture that is supported by only one relatively small company.

All this leaves U.S. supercomputing hopes pinned for the most part on entirely new architectures—those that may have the potential to outperform vector computing. Although DARPA's grants were initiated in response to the Earth Simulator, they are meant to achieve a fundamentally different goal: to make super-

Current and Proposed Supercomputer Architectures

ARCHITECTURAL APPROACH	DESCRIPTION	ADVANTAGES	MAIN PROPONENTS
Commodity clusters (operational)	Hundreds or thousands of off-the-shelf servers with low-bandwidth links	Low-cost construction; efficient with problems that can be broken into chunks	Hewlett-Packard, IBM, Silicon Graphics
Vector computing (operational)	Hundreds of custom-built processors with high-bandwidth connections	More time spent computing, less time communicating	Cray, NEC
Streaming (experimental)	Intermediary values of calculations stored in local memory	Speed; on-chip data transfer for reducing the "memory bottleneck"	Stanford University
Processor-in-memory (experimental)	Processing circuits and short-term memory interspersed on the same chip	Speed; shorter distance between processors and memory	University of Southern California, Caltech, IBM
Cascade (experimental)	Data, rather than software, held in processors' local memory	Fewer calls to memory in cases where data sets are larger than programs	Cray, Caltech

computers that are not only faster, but also cheaper to build and use than anything previously developed. Is there a way to do this all at once? It's logical to think there should be, but the answer is not apparent. "We're starving in an era of plenty," says Bill Dally, professor of electrical engineering and computer science at Stanford University. "All the ingredients for computing—arithmetic, communications, memory—are getting cheaper, and for almost anything besides [high-performance] computing, costs per unit get cheaper as you scale."

instead? They are willing to share their optimism, but Smith and Sterling say little else about their nascent architecture. "I'm purely subjective, but I think it's the most exciting thing in high-performance computing in the last 20 years," says Sterling.

These are the proposals eliciting the most interest at the government agencies likely to be buying the high-performance systems of the future. But for the most part they are prototypes, or even less, and they will prove themselves only after radical changes are made in everything from processor design to the way software is engineered. Then the challenge will remain to find a way to manufacture the new systems efficiently and without defects. In other words, these ideas offer no quick fix.

The United States won't be at the cutting edge of simulation—the "third pillar" of scientific discovery—if the performance of its computers lags.

As with any new architecture, the greatest challenge will be the memory bottleneck, where data's comparatively slow trek to and from memory hampers processor efficiency. Even as it continues to pursue its own vector-computing systems, Cray is attacking that problem by adapting the interprocessor communications techniques used in the Earth Simulator to increase data flow in Red Storm, a massively parallel computer to be built at Sandia National Laboratories in New Mexico.

Dally believes he has developed another solution, which he calls "streaming." While traditional computing architecture treats all arithmetic operations equally, the calculations in many scientific simulations build on themselves, with no need to store intermediary values in long-term memory. So rather than passing control from one instruction to another and accessing memory sequentially, Dally is building a system that streams data to processors, which then act on the problem locally through many intermediate calculations and stream the finished values back to memory. "Protein folding is an example where to understand how two molecules interact, you need to carry out perhaps 500 intermediate results before arriving at the one you want," says Dally. "With streaming you can capture those intermediary results in local registers where the communications bandwidth is very inexpensive, and you never touch the memory system."

Advances in microprocessor-manufacturing techniques are also making it possible to put processors and large amounts of memory on the same chip, shortening the distance that instructions and data must travel. IBM plans to try such processor-in-memory techniques in supercomputing, and DARPA is funding an effort at the University of Southern California to explore exactly how processor-in-memory technology can improve high-performance systems. Researchers at the University of Southern California are working with Hewlett-Packard to deliver an experimental system to DARPA for evaluation. And a project at Caltech known as Gilgamesh is examining the best way to arrange memory and logic together on a chip: if small blocks of memory and logic were interspersed around a chip, for instance, travel time would continue to drop, enhancing performance.

Another option is simply to turn the entire architecture on its head. Cray's Burton Smith and Caltech's Sterling are cooperating on a DARPA-funded project they call Cascade. The two are investigating ways to exploit the fact that in high-end scientific computing, the heft of the data alone is often far greater than the heft of the application program. In other words, if the stuff stored in memory is so much larger than the program needed to run it, why move it at all? Why not move the program to the memory

Computing's Apollo Project?

For the last decade, the U.S. high-performance-computing community has been standing on the shoulders of giants. Many directors of centers for scientific computing say they believe the United States is at a critical decision point, where choice of projects and the amount of funding invested in new high-performance-computing architectures could affect future security and prosperity in tangible ways.

"It's really going to take a combination of good ideas coming out of universities and government funding and good industrial engineering to address this nasty problem," says Bell. "Building a new chip is right at the hairy edge of what a university can accomplish; then you need someone with the resources to do detailed engineering stuff like cooling and connections and so on. It's going to take a lot of effort."

But if it's done right, an entirely new golden age of science could flower. One of the most striking aspects of the Earth Simulator project is its openness. Scientists are communicating despite language and geographical barriers. They are testing theories and conducting simulations that have the potential to improve our understanding of the world and benefit all of us. A few months ago, Sterling brokered a meeting between Tetsuya Sato, director of the Earth Simulator facility, and John Gyakum, a McGill University professor who is one of the world's leading experts on the ways small weather systems such as thunderstorms affect global weather patterns. Before the Earth Simulator there had been no computer that could easily factor such small systems into large-scale climate simulations. Now there may be. "They have opened themselves to collaboration because they care above all about scientific results," says Sterling. "And what they're doing is important to everyone on the planet."

So it's not just to advance computer science that more and smarter computing is required. It's to advance every science. "Science in the 21st century rests on three pillars," says the Energy Department's Decker. "As always, there's theory and experiments. But simulation is going to be the third pillar for scientific discovery. Given the problems we're faced with, we clearly want to be at the cutting edge with our science. If the performance of our computers is an order of magnitude less than what we know they can be even today, then we won't be." TR


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Personalized Medicine's

Bitter Pill

BY STEPHEN S. HALL ILLUSTRATIONS BY BRIAN CAIRNS

New genetic data will lead to safer and more effective drugs customized to individuals. But society will have to rethink the business and ethics of medicine.

If it were not for the great variability among individuals," 19th century physician William Osler observed, "medicine might as well be a science and not an art." There will always be room for art in medicine, but the advent of diagnosis and treatment based on molecular knowledge of diseases is shifting the equation decidedly toward science. Almost from the moment the Human Genome Project completed its draft sequence in 2000, the intimate genetic knowledge it conferred has been accompanied by promises of a powerful, customized form of medicine. Visionaries talk of people carrying their entire genetic sequences on personalized CDs, of medicine artfully tailored to individual anatomies, and of diagnostic tests' predicting who is likely to respond to a particular medicine, who is likely to react badly, and who is unlikely to benefit at all.

Armed with details of individual variation, biologists could parse patients into subgroups and predict which is likely to have an aggressive or indolent form of a disease and which would respond to one drug rather than another. Allen D. Roses of GlaxoSmithKline and Duke University School of Medicine has predicted that this approach, called pharmacogenetics, "will change the practice and economics of medicine," and the popular media have picked up and amplified that message. In 2001 *BusinessWeek* hailed personalized medicine as an idea that "has captured the imagination of biotech futurists," and *Newsweek* suggested that "if pharmacogenetics works, the days of one-size-fits-all therapy could go the way of bleeding by leeches."

A technology that identifies who will benefit from a treatment automatically identifies who *won't* benefit too.

But underneath those extravagantly rosy and somewhat wishful predictions lie important scientific, economic, and societal questions, beginning with one of feasibility. David Altshuler, director of the Medical and Population Genetics program at MIT's Whitehead Institute and an endocrinologist at Massachusetts General Hospital, points out that personalized medicine remains "a model, a hypothesis" of the way medical care will evolve. "The genome is going to empower all sorts of things, but it's not going to happen for 20 years," he says. Along the way, personalized medicine is likely to raise a number of prickly issues: foremost among them is the paradox that the more personalized the medicine, the less interesting the business. As numerous observers have pointed out, big pharmaceutical companies have become addicted to blockbuster drugs. Targeting a smaller subgroup of a patient population by definition focuses on a smaller market.

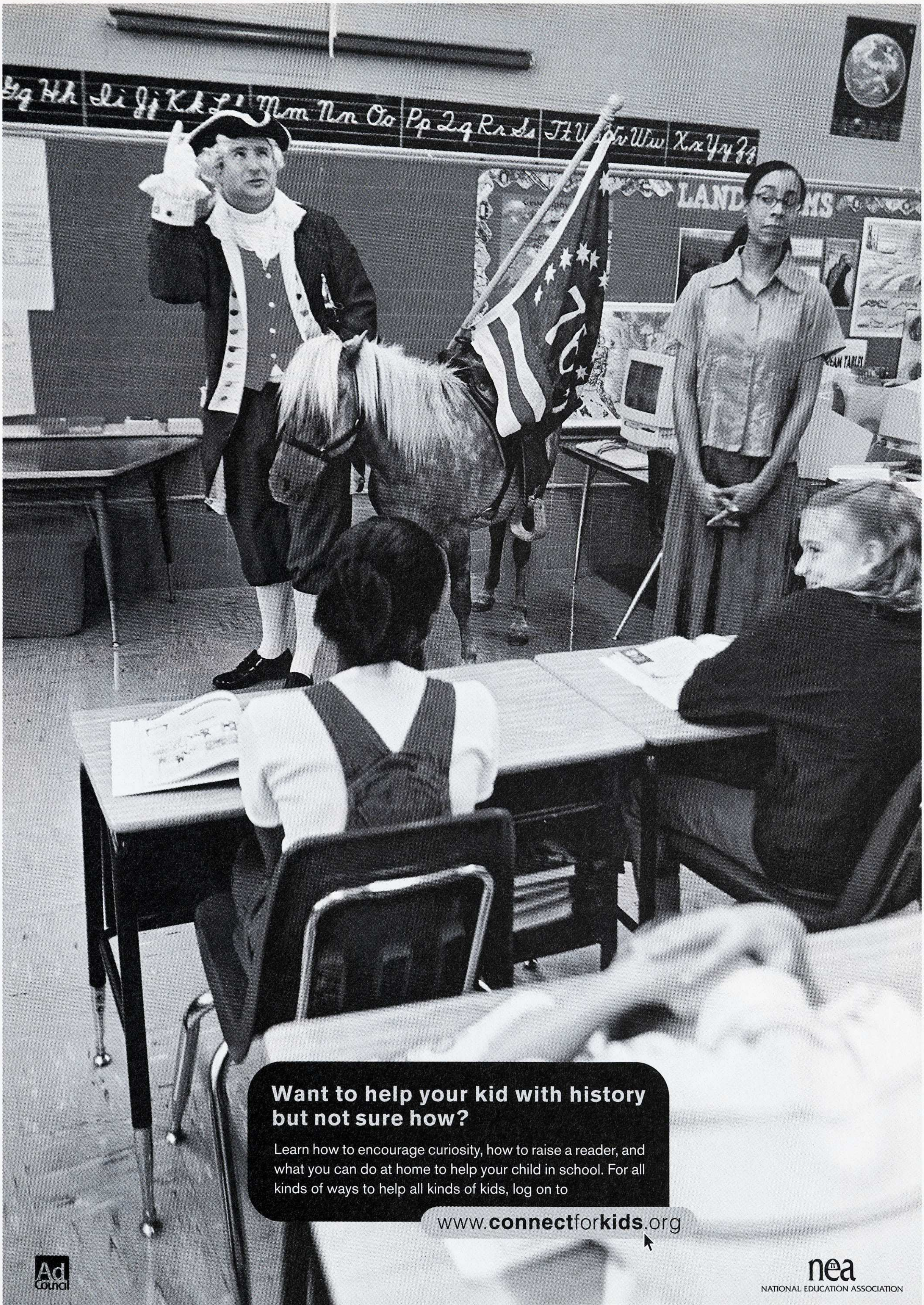
Theoretically, one economic advantage of personalized medicine is that clinical trials might be conducted more efficiently and with a greater chance of success when researchers can so specifically select patients for testing. But how small does the pie of potential patients have to shrink before it ceases to be economically viable? Furthermore, personalized medicine is not without social implications. A technology that identifies who will benefit from a new treatment automatically identifies who *won't* benefit too.

Researchers, venture capitalists, and economists have been gnawing on these questions and wondering how the field of personalized medicine actually will evolve. Despite the compelling science, some investors find that the economics still leave a lot to be desired—at least in the short term. A venture capitalist who requested anonymity notes, "The vision of personalized medicine is that you'll go to your doctor's office, get your finger pricked, give a drop a blood, and it will be put in a machine—right there in the office—which will tell you what drug is going to work for you. But we haven't seen very many companies that have a viable business model in this area."

The view from the lab is different. "The treatments we currently use to treat most patients are grossly ineffective. In type 2 diabetes, many people don't respond," says Altshuler. "If it were true that you could identify five to 10 percent of the market, identify and treat them in a controlled and perfected way, I think it would be a wonderful thing, and I think you could make money on it too."

BUMPY ROAD

Given the uncertainties, those starting down the road of personalized medicine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could well learn from Genentech, the South San Francisco, CA, biotech pioneer, and its experience creating a cancer drug called Herceptin. Few people made the connection at the time, but Herceptin's development—from the discovery of a surface marker on breast cancer cells in 1982 to the U.S. Food and Drug Administration's approval of a drug targeting that marker in September 1998—is a useful study of the financial risks, clinical problems, social ramifications, and rich rewards of personalized medicine.

The defining characteristic of every form of personalized medicine is its biomarker, a kind of biological fingerprint that distinguishes a subset of the patient population. Herceptin is based on a marker protein that sits on the surface of malignant cells. Called neu when it was first discovered by Robert Weinberg's group at MIT in 1982 and more popularly known as Her-2 following its independent isolation in 1985 by Genentech scientist Axel Ullrich, the molecule "listens" for signals that tell a cell to grow and multiply. Large numbers of these receptor molecules turn out to be present in certain aggressive breast cancers because the gene for the receptor is "overexpressed."

As early as 1987 it had become clear that only 25 to 30 percent of women with breast cancer overexpressed the Her-2 gene and might benefit from a drug that blocked the growth signal. But by 1990 scientists at Genentech had developed a drug that would block the Her-2 protein and theoretically would block growth signals to a cancerous cell. "We weren't really thinking of it in terms of individualized medicine back then," says Debu Tripathy, an oncologist at the University of Texas Southwestern Medical Center who participated in the early testing of the drug at the University of California, San Francisco.

With a biomarker in hand, researchers can identify a subgroup more likely to respond to a drug during clinical trials, but the biomarker also segregates the patient population. "Never underestimate the desperation of a patient to obtain a drug," observes Jan Platner of the National Breast Cancer Coalition, "whether she qualifies for a clinical trial or not." That lesson of personalized medicine was learned for perhaps the first time, and certainly the hard way, by Genentech.

The company employed a diagnostic test to screen breast cancer patients to see whether they had the Her-2 marker and thus qualified for trials of the experimental drug. Safety studies began in 1992, and the first, small-scale efficacy studies were completed by 1994. Although the results were preliminary, several women with advanced cancers responded dramatically, and word began to spread through the breast cancer underground. A number of women demanded that their tumors be tested to see whether they would qualify for the experimental drug.

One of those women, Marti Nelson, was a physician from Vacaville, CA. For months, Nelson tried unsuccessfully to get the Her-2 diagnostic test. By the time she finally was tested and learned that her tumor was indeed Her-2 positive, she was terminally ill. She died in November 1994. Her death—and her inability either to get tested or get the experimental drug—crystallized the frustration of women with breast cancer. Whether they had the biomarker or not, whether there was enough of the drug to go around or not, breast cancer patients began to demand access to Herceptin.

In December 1994 several dozen protesters got into their cars and formed a "funeral cortege" to honor Marti Nelson. They encircled Genentech's headquarters and blocked the parking lot. They leaned on their horns and activated car alarms. They drove up on the lawn in front of the company's headquarters. Some protesters, many with advanced metastatic cancer, handcuffed themselves to the steering wheels of their cars. The long, unending wail of horns became a kind of plaintive scream on behalf of breast cancer patients who demanded not only access to the drug, but also a role in designing clinical trials and evaluating the data. "It was really that demonstration and the public attention that followed that forced Genentech to sit down at the table," recalls Barbara Brenner, executive director of Breast Cancer Action, a breast cancer awareness group. "We'd never had anything like that before," agrees Jennifer

A Better Diagnosis

Researchers at universities and biotech and pharmaceutical companies are racing to realize the promise of personalized medicine. Using rapidly improving tools of molecular biology, such as DNA chips that allow biologists to analyze which genes are on or off in malignant or diseased tissue, drug researchers are scrutinizing molecular data for biomarkers that characterize subpopulations of patients. One early conclusion: many deadly diseases actually exist in several molecularly distinguishable forms. By recognizing these differences among groups, researchers hope to better understand why patients respond differently to treatments.

In 2000, for example, Jeffrey Trent at the National Human Genome Research Institute in Bethesda, MD, teamed up with researchers at Agilent Labs in Palo Alto, CA, to examine several types of cancer. The researchers used gene chips to assess the expression patterns of more than 6,000 genes in tumor tissue—including tissue from 31 patients with the skin cancer melanoma—and correlated the patterns with the disease's progression. "The patients look the same," says Stephen Laderman, manager of the molecular diagnostics department at Agilent Labs' Life Science Technologies Laboratory, "but they respond to treatment differently." The groups discovered in 19 patients a pattern of gene expression that correlated with a less invasive form of the disease. "They were able to distinguish, on the molecular level, these patients from other patients," says Laderman, "and it was correlated with the behavior of the tumor." The two labs have mounted a similar effort to distinguish genetic profiles of patient subgroups with breast cancer and sarcoma.

These labs are hardly alone. Millennium Pharmaceuticals, in Cambridge, MA, has identified a set of genes in ovarian cancer that predicts which women will fail to respond to the standard, highly toxic, treatment. While this approach does not immediately provide a new therapy, the technology nonetheless advertises one of the goals of personalized medicine: sparing patients the distress of useless treatments that cause nasty side effects.

Researchers at Genaissance Pharmaceuticals in New Haven, CT, meanwhile, have already launched studies to identify genetic profiles that correlate with good responses to existing drugs for asthma, schizophrenia, and high cholesterol. As was the case with Herceptin, the results could lead first to diagnostic tests that identify differences in patient groups and ultimately to drugs tailored to the newly recognized groups.

Bryson, Genentech's director of patient advocacy issues. "And that's certainly what got our attention."

In some respects, the Herceptin case was simply another example of cancer patients clamoring for a new drug, but it became complicated by the molecular marker that made some patients eligible for clinical trials and others not. Genentech was concerned that including patients who lacked the Her-2 marker would dilute the power of the trials' statistics to show that the drug worked; indeed, subsequent estimates suggested that if Herceptin had been tested in the general breast-cancer population, only about six percent of the patients would have shown a response, which would have made it seem a marginally effective drug.

Yet patients view potentially lifesaving drugs not rationally, but emotionally. Patient activism nearly torpedoed Herceptin. Just as Genentech was designing its final, pivotal trial to establish whether Herceptin was truly efficacious against breast cancer, activists mounted a campaign, demanding that the company give them increased access to the drug and a role in planning the drug's trials. Genentech officials demurred, expressing concern that such access would skew the results and asserting that, in any event, there wasn't enough of the drug to go around. "From the political and sociological standpoint, that was just a very difficult time," says oncologist Tripathy.

In the summer of 1995 Genentech launched its final, large-scale trials of Herceptin and immediately ran into trouble. During the first five months, only 14 women signed up for a trial slated to enroll 450. In August Genentech announced it would provide compassionate access to the drug and sought the help of breast cancer advocacy organizations to get the trial back on track. Patient advocates ended up helping to redesign the trial, and they worked closely with the company on patient accrual, data assessment, and monitoring. They were, Bryson says, "very, very helpful." And with the selective power of the diagnostic test, Genentech completed its final trial ahead of schedule, despite the sluggish start.

SPLINTER GROUPS

The Herceptin case offers multifold lessons for personalized medicine. But perhaps the most critical of those lessons concern what might be called the sociology of diagnostics. For all its power to help doctors target treatment, the precision of molecular genetics can easily generate a residue of medical frustration. "What do you say to someone who doesn't qualify for the drug?" asks the National Breast Cancer Coalition's Platner. In that sense, developers of personalized medicine can inadvertently dispossess subgroups of patients. And as its power to fractionate increases, personalized medicine could have the unintended effect of creating many slivers of groups too small to warrant the economics of further drug development. One patient advocate says, "The downside is: What about something that's very effective, but only for one percent of the patient population? Is that going to be developed?"

What about a drug that's very effective for only one percent of patients? Is that going to be developed?

Scientists at the National Human Genome Research Institute are exquisitely aware of the possibility of such problems. "The role of government is to work on the fragments of the patient populations that pharma isn't going to pick up," says one government researcher who has been participating in the development of the institute's five-year plan. "Those discussions are still early, but that is already a concern, and it's a real issue."

Another collateral issue of personalized medicine is the accuracy of the diagnostic tests. Yet again, the Herceptin example offers a cautionary lesson. The first test that was developed to measure a woman's Her-2 status typically identifies 10 to 20 percent of patients incorrectly, says Tripathy. In other words, the diagnostic was hardly definitive, and both false positives and false negatives caused a lot of frustration among breast cancer patients. Last August the FDA approved the use of an improved gene-based test for determining which patients qualify for Herceptin. The new test is "probably a little more accurate," says Tripathy. But in that no man's land between statistics and human emotion, the lives of many patients may be convulsed by inaccurate diagnoses. "I can foresee that happening with a lot of drugs, where the diagnostic doesn't give a simple yes-or-no answer," says Platner.

Even an imperfect diagnostic test, however, can give a rough answer to another important nonmedical question: it can identify the potential size of the market, a factor big pharma is considering earlier and earlier in the drug development process. In the cold, hard arithmetic of marketing, the fact that only 25 to 30 percent of breast cancer patients possess the Her-2 marker basically quarters the universal market of 180,000 women who are diagnosed with breast cancer each year. Robert Bazell's book, *Her-2*, a definitive account of the development of Herceptin, describes the initial skepticism inside Genentech. John Curd, then a medical director at the company, believed Herceptin's hypothetical market did not justify the more than $150 million it ultimately took to get it there; Bazell's book quotes Curd as saying that "today if Her-2 came forward, you couldn't get it into development." But oncologist Tripathy says, "I think Genentech's thinking was, 'Look, it's still 20 to 30 percent of the breast cancer market, and that's still a big market.'" Genentech's Bryson adds, "We have often done work in very small patient populations. Genentech employees are very ideologically motivated, and part of our mission is unmet medical need."

Each company is likely to have its own answer to the question of whether a targeted patient population is too small, but every answer is an economic work in progress and doesn't necessarily stem strictly from market size. "To be honest, we're still trying to get our arms around this issue," says Geoff Ginsburg, vice president of molecular medicine and research strategy at Millennium Pharmaceuticals in Cambridge, MA. Personalized medicine's advantages, he suggests, are as much qualitative as quantitative. A targeted treatment allows a more focused clinical trial, which if it is successful, permits a company to charge "premium prices," particularly for a drug that is highly effective against a grave and often


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fatal illness. Herceptin treatment, for example, costs about $3,000 a month, and many patients are on it for years. Personalized medicine also allows a company to establish a therapeutic beachhead in a disease population, with opportunities to expand the market. And it offers advantages to patients: patient compliance is likely to increase, says Ginsburg, if there are data suggesting that the patient is likelier to respond to treatment.

Another possibility, more humanitarian than economic, is that patients will be spared highly toxic treatments if, say, genomic analysis indicates they won't respond to chemotherapy. And Ginsburg believes that focusing on the nonresponder population might eventually provide clues for developing treatments that apply to the entire patient population. But even success would introduce its own set of problems. Altshuler says that "one of the hard issues we'll have to confront is *not* treating people because they won't benefit. If a treatment is working on some people and not others, are we going to be saying to patients, 'I'm not going to even let you have a chance to respond'? That's not how we usually do things."

PROMISE AND PERIL

The Herceptin story offers an encouraging epilogue about the development of small-market drugs. Annual sales of the drug began modestly at $188 million in 1999. But sales have climbed steadily to about $346 million in 2001, and Genentech has deftly marketed the drug and expanded its possible uses. Originally approved for patients with the Her-2 marker who had developed metastatic breast cancer and had failed to respond to all other forms of chemotherapy, Herceptin is being tested as supplementary therapy following surgery for breast cancer and in cases of ovarian and lung cancer in which Her-2 is overexpressed.

Rituxan, an anticancer drug developed by IDEC Pharmaceuticals and marketed by Genentech, has followed a similar pattern. The FDA approved the drug in 1997 for non-Hodgkin's lymphoma, a cancer that affects certain immune-system cells with a surface marker called CD-20. That marker allows for a targeted attack on malignant cells. Genomic analysis is identifying gene expression patterns that correlate with the disease's progression; such analysis will ultimately affect treatment decisions. From initial sales of $162.6 million in 1998, its first full year on the market, Rituxan racked up sales of $818.7 million in 2001 and was well on its way to becoming a billion-dollar drug with expanded use by the end of 2002. The cells targeted in non-Hodgkin's lymphoma may play a role in other diseases, such as chronic lymphocytic leukemia and rheumatoid arthritis, so the market may well extend even further.

So the pioneering drugs of personalized medicine convey messages of both caution and promise: Caution about the effect targeted biomarkers can have on a patient population, as well as the way the reaction of those patients can in turn influence the testing of drug candidates and the public's perception of a company. Promise that a patient population can be identified and treated with a targeted drug that offers greater efficacy, as well as that nonresponders may be spared the ravages of toxic, ineffective treatments. And promise, too, that even a drug targeted to specific biomarkers can have economically bright prospects. The trick will be to capitalize on the promise without leaving too many disenfranchised patients behind.

As bumpy and fitful as was Herceptin's journey to market, it serves as an inspiration to latter-day practitioners of personalized medicine. "I'm sure Genentech was having to wrestle with the decision of, 'If only 20 to 25 percent of the population responds, how are we going to compete?'" says Millennium's Ginsburg. "But somebody had to be first, and I think it's great that they did it."

Despite the economic challenges and societal issues associated with personalized medicine, its role in the future of medical care seems all but assured. Not only is personalized medicine going to happen, argues Stephen Laderman, manager of the molecular diagnostics department at Agilent Labs' Life Science Technologies Laboratory, in Palo Alto, CA, but it is going to happen soon, in part because more and more patients are learning to demand whatever knowledge will empower their decisions about disease treatment. As patients learn more about their options and researchers learn more about the molecular specifics of their patients' diseases, personalized medicine may still be a bitter pill for many to swallow, but it will be one well worth taking as an antidote to the ravages of disease. TR

Timeline

1985
Axel Ullrich, a Genentech researcher, clones the Her-2 receptor.

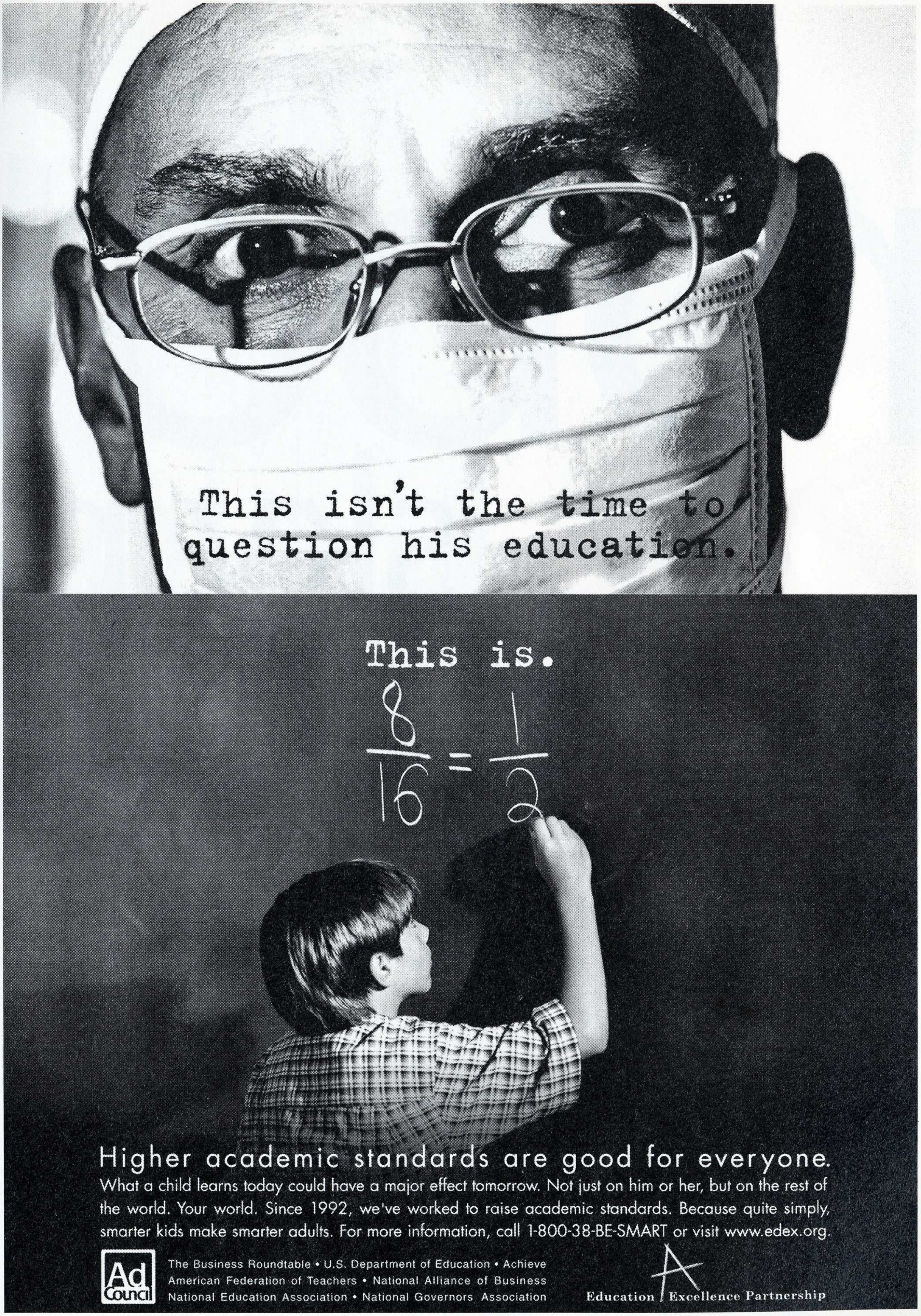
1998
Using the Her-2 marker, Genentech selects hundreds of patients for its clinical trials of a targeted breast cancer therapy and wins FDA approval.

2001
Gleevec, an anticancer drug developed by Novartis, receives FDA approval for treatment of leukemia patients with a specific gene mutation.

1980 — 1997 — 2000

1999
Todd Golub of the Whitehead Institute, collaborating with Affymetrix, shows that gene chips can be used to analyze the molecular characteristics of cancer tissue.

2000
The Human Genome Project completes a draft sequence of all human genes.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DEMO

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THE MILITARY'S REMOTELY PILOTED PLANES MAKE IDEAL SPIES— BUT EACH ONE COSTS MILLIONS. STANLEY HERWITZ THINKS OFF-THE-SHELF TECHNOLOGY CAN MAKE AERIAL SENSING AFFORDABLE FOR EVERYONE.

PHOTOGRAPHS BY EMILY NATHAN

Wake up and sense the coffee. One day last September, that was the job of a research team led by Clark University earth scientist Stanley Herwitz, a proponent of low-cost wireless aerial imaging for the masses. Rising well before dawn, Herwitz's team rolled Pathfinder Plus, a solar-powered unmanned aerial vehicle (UAV) from NASA, onto a U.S. Navy runway on the island of Kauai, HI, and launched the plane into the sunrise. They guided the craft by radio to a height of 6.4 kilometers over the rapidly ripening fields of Kauai Coffee, the largest U.S. coffee plantation. There, commercial cameras under the UAV's wing snapped digital photos of the fields at both optical and infrared frequencies and transmitted them in near-real time to image specialists who used them to identify the ripest plants and guide harvesting machines. The plantation managers "were real happy with getting a complete view of their fields," says Herwitz, whose proposal for a UAV science mission beat 45 others in a NASA funding competition. His hope, he told *Technology Review* senior editor Wade Roush, is that UAVs will circle continuously over inhabited areas, relaying images that could be used to plan farm irrigation, reduce traffic jams, manage wildfires, and direct disaster relief. "Everybody associates UAVs with the Department of Defense," Herwitz says. "Defense may invest in this, but the reality is there will be some positive commercial uses of these aircraft."

It's a bird, it's a plane: Stanley Herwitz on the tarmac at NASA Ames Research Center, a test site for his imaging pods.

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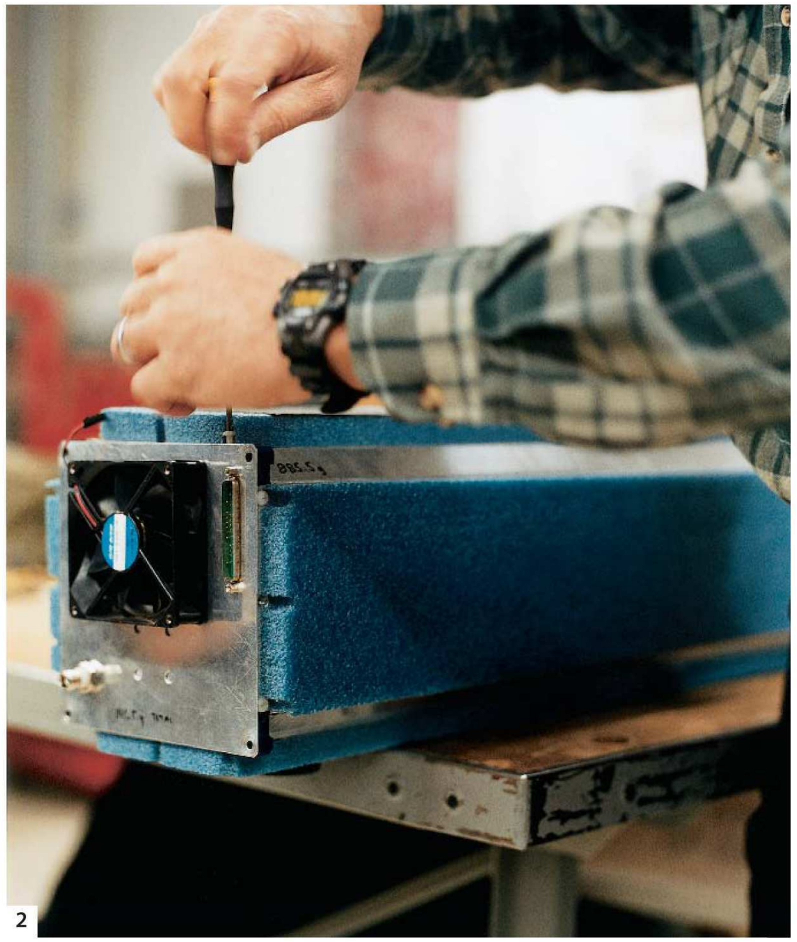

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1-4. POD PEOPLE. Two members of Herwitz's coffee project—NASA aerospace engineer Stephen Dunagan *(left in image 3)* and instrument specialist Robert Higgins *(right)*—re-create the assembly of one of the instrument pods used in the Kauai test. The fiberglass shell *(1)* includes wiring for external-temperature sensors. Dunagan attaches the aluminum-and-foam outer casing *(2)* for the payload that will fit inside the shell: the mission's imaging and communications hardware. Inside are a $10,000 DuncanTech camera with three digital-image collectors to gather data at visible and infrared frequencies; a Linux-based computer to run the camera; and a wireless Ethernet "bridge," or transceiver, from Cisco Systems to transmit images to a directional antenna on the ground. Dunagan and Higgins slide the shell over the instrument casing and attach the front cap, making the pod airtight *(3 and 4)*. The camera's lens is visible through a glass window. At the back of the pod is a finlike omnidirectional antenna with a range of more than 20 kilometers.

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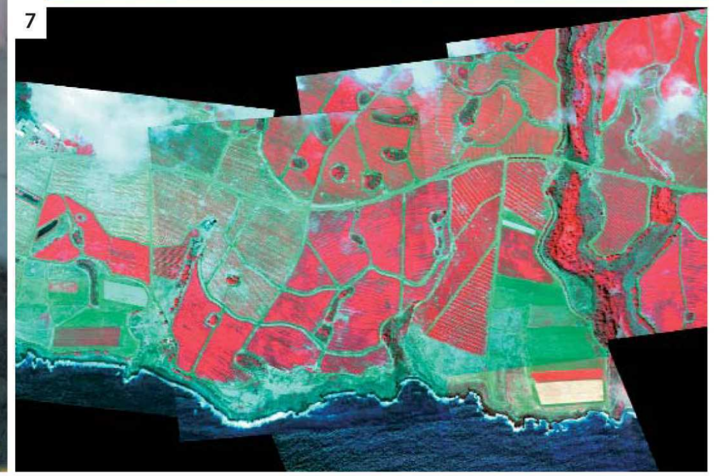

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COURTESY OF STANLEY HERWITZ

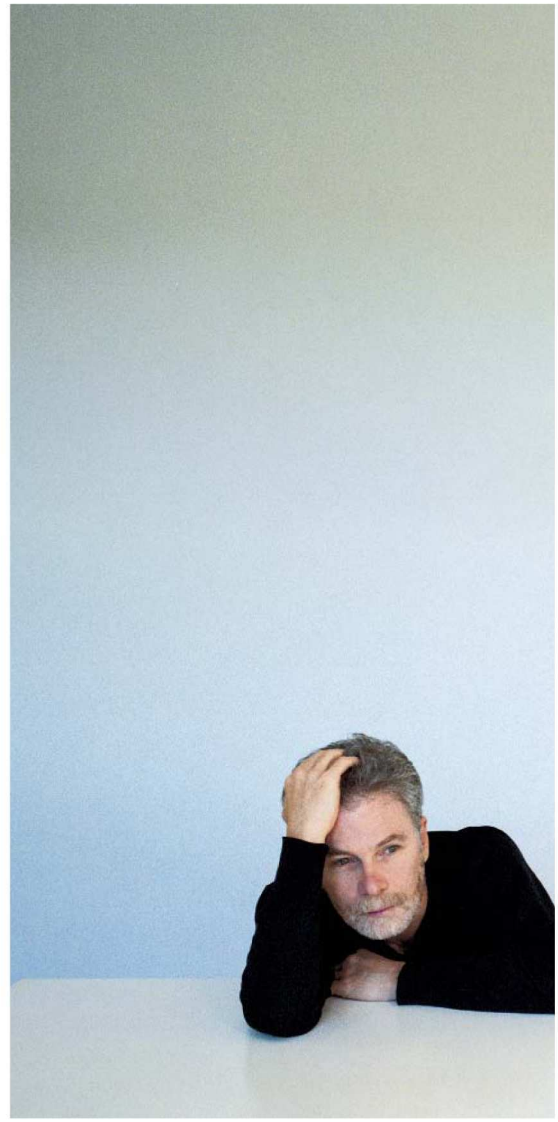
5. UNDER MY WING. In a picture taken in preparation for the flight day last September, Dunagan and Higgins attach the pod carrying the DuncanTech camera to the "flying wing" of the Pathfinder Plus. A sister pod carries a Hasselblad studio camera with a Kodak digital back, used to collect full-color images.

6. SOLAR SAILOR. Pathfinder Plus quickly gains altitude. The top of the craft's 37-meter-long wing is covered with solar photovoltaic cells, which power the eight propellers and the equipment in the pods (visible under the wing's midsection). Herwitz is at first dismayed to find that the coffee plantation is mostly hidden under low clouds. "But," he says, "we were able to guide the plane to openings and piece it together. So we were really mosaicking—with almost 70 to 80 percent cloud cover—a composite image of the area of interest. When we were done, I realized the clouds were a welcome challenge. You really can show the value of the plane to be able to loiter." Right now the Pathfinder Plus must land when the sun goes down, Herwitz says, but in the future UAVs with solar-energy storage capability will stay aloft for days, weeks, or months.

7. CONDITIONS ARE RIPE. Good timing is crucial in the coffee business; coffee cherries picked before full ripeness yield beans that fetch a lower price. That means growers must collect sample coffee branches manually, gauging the fields' readiness by their color. Using this multispectral photo, however, harvest managers at Kauai Coffee could see that the ripest cherries (bright red in the image) were in the plantation's eastern section, to which harvesting machines were quickly deployed. The team's success spotting Kauai's ripest coffee cherries, Herwitz believes, will give a jolt to other forms of precision agriculture, as soon as UAVs themselves become more affordable. "Could the coffee people pay for it?" he asks. "Someday, yes. Once these craft can stay aloft for long periods, they will be cheaper than manned aircraft. It would really be like giving farmers access to imagery from a mobile satellite." TR

By Erika Jonietz | Photograph by Sian Kennedy

CHOOSING OUR CHILDREN'S GENETIC FUTURES



Gregory Stock

POSITION: Director, University of California, Los Angeles, Program on Medicine, Technology, and Society

ISSUE: Designer babies. Advances in biology and medical technologies are pushing the frontiers of genetic engineering to the point where the possibility of parents' selecting specific traits for their children is closer to science fact than fiction.

PERSONAL POINT OF IMPACT: Author, *Redesigning Humans: Our Inevitable Genetic Future*

TECHNOLOGY REVIEW: You claim that parents will be able to genetically enhance their unborn children. But how realistic is the idea of genetically engineering embryos, eggs, or sperm—our "germline cells"—to create designer babies? It sounds like science fiction.

GREGORY STOCK: For the immediate future, it is. You have to have two things first: something worth doing and a safe, reliable way of doing it. At present, neither exists. There really are no platforms for doing reliable, safe interventions of this sort. And even if you had a safe way of inserting genes, you wouldn't have anything to do, because we don't know enough about our genetics to accomplish anything that would be worth whatever risks are involved.

But that doesn't mean that such modifications are particularly distant. Both those requirements, I expect, will be met within the next generation, so it's good to start thinking about these sorts of things now. The potentials will arrive quickly once the technology moves forward.

TR: In what ways are people already starting to confront the ethical issues associated with choosing children's genetic fates?

STOCK: We are beginning to open up our biology and intervene in realms that have always been beyond our reach. Well before the technology of germline intervention itself is ready for prime time, we'll be dealing with sophisticated screening that allows prospective parents to use genetic tests to pick and choose among their embryos. Preimplantation genetic screening already has been used with in vitro fertilization for a decade to avoid serious genetic diseases like cystic fibrosis. Parents test their embryos for the mutation and discard those that are afflicted. Soon, such testing will move to a broad array of potential genetic diseases, then to lesser vulnerabilities like a heightened risk for severe depression, and then to nondisease traits—choices about temperament and personality.

The controversies provoked by these capabilities and how parents use them will be very similar to the ones we will face in manipulating the germline directly. Functionally, there's little distinction between going in and modifying a gene to correct a mutation that will cause Huntington's disease and simply screening to avoid that mutation; or between picking an embryo with certain potentials and adding genes to create them. So I see this as a broad policy debate that is less about a particular technology than about the capacity for parents to make choices about the genetics of their children.

TR: What kinds of traits will it be possible to engineer? Are parents going to be able to pick the height, intelligence, or musical talents of their children?

STOCK: Right now we don't know what's going to be too complicated to do and what will be very, very easy. I think we'll be surprised at the numbers of things that turn out to be easy. Certainly, there have already been complex traits—ones undoubtedly shaped by many genes—that can be substantively altered by changing one gene. Researchers have modified single genes to roughly double the life span of fruit flies and roundworms. And there was recently an astonishing study where researchers changed one gene in mice, and it greatly enlarged their brains and gave them a wrinkled, deeply folded surface similar to that of the human brain instead of the smoothness typical of a mouse. When medical science begins to understand our genetics, it will become possible to screen for various constellations of genes that will likely bring beneficial effects—tendencies towards vitality and health or various personalities and predispositions we like. And once we start using such information to choose embryos, it won't take us long to start thinking seriously about just going in and creating those sorts of genetic constellations directly.

TR: You speak of "our inevitable genetic future." Won't numerous groups want to limit if not outright ban such technology?
STOCK: No matter how much we discuss these things, we're not going to reach a consensus about what should be done. These issues touch our values too deeply, hinging on culture, religion, and philosophy. Those who want to stop such technology do not want to do so because they think it may go awry and cause injuries, although that's what they say. They want to stop it because they fear it will be wildly successful and sweep humanity toward a pernicious future. And they feel an urgency to stop such technology now, before it even arrives, because they're afraid that if we get too much benefit from it, then too many people will see it as desirable. For example, you would be hard put to ban in vitro fertilization now: too many children are here because of the technology; too many happy parents would be childless without it. And it could be the same with many of these other technologies.

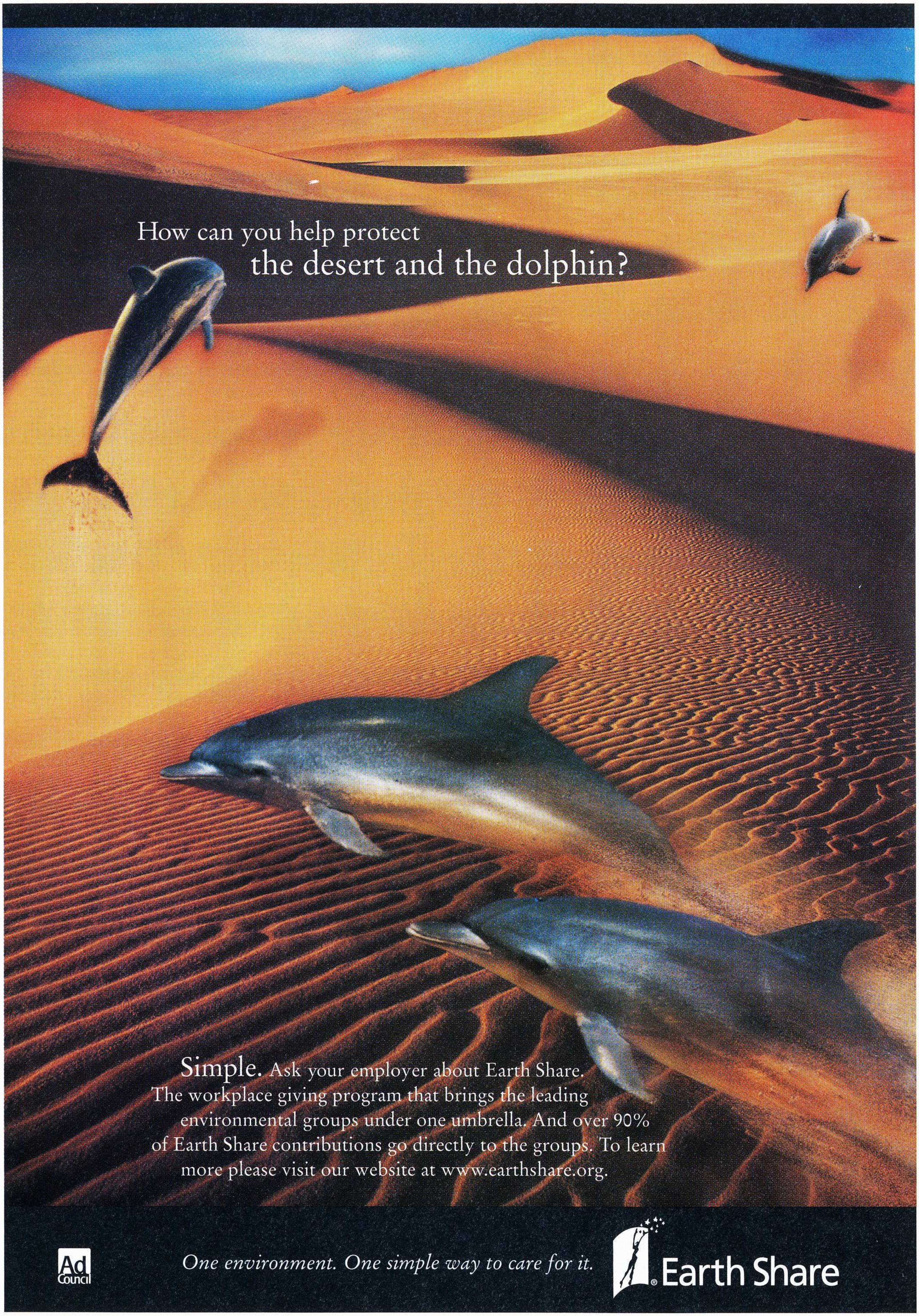
I don't believe it will be possible to stop germline intervention. But the politics will have impacts on where breakthroughs are made. A good example is therapeutic cloning—the work on embryonic stem cells to treat Alzheimer's, diabetes, and other diseases. Even though the 2002 attempt to ban this in the United States failed, the associated uncertainty has made this country a very problematic environment for doing this sort of work. So a number of researchers have moved overseas: there are strong efforts in Britain, Singapore, and Australia. The U.S. government could not halt these technologies, even if it wanted to. We can make a lot of noise about particular clinical applications, but ultimately we should remember that this will happen because these potentials are really just spinoffs of mainstream medical research that we all want.

TR: Creating designer babies seems like a procedure that, at least for a while, will be restricted to the wealthy. Will this be a biological equivalent of the digital divide?
STOCK: All these technologies tend to be available initially to the more affluent and more motivated. That's the way it works with every technology. In vitro fertilization was enormously expensive a decade and a half ago. And now, it's come down to where a person can go through an IVF procedure for $6,000 to $8,000, which is not inexpensive but is certainly well within the means of a vast number of families in this country. There are about 25,000 kids born by IVF in the U.S. every year. And if you compare it with the cost of a car, it's affordable.

These early users do us a great service. They test these technologies for us and even pay enormous sums for the privilege. In a way, they function as guinea pigs for the rest of humanity. If you had to think of who you'd like to test these technologies, what better group can you imagine? They're well informed, highly motivated, eager, hard to coerce, and they are definitely volunteers.

I think the biggest gulfs will not be between the rich and the poor of one generation, but between one generation and the next generation and the next generation after that. This is because what is available today is so very primitive compared to what will be available 25 years from now, and that too will seem primitive after yet a further 25 years. TR

For an expanded version of this interview, go to www.technologyreview.com/impact/.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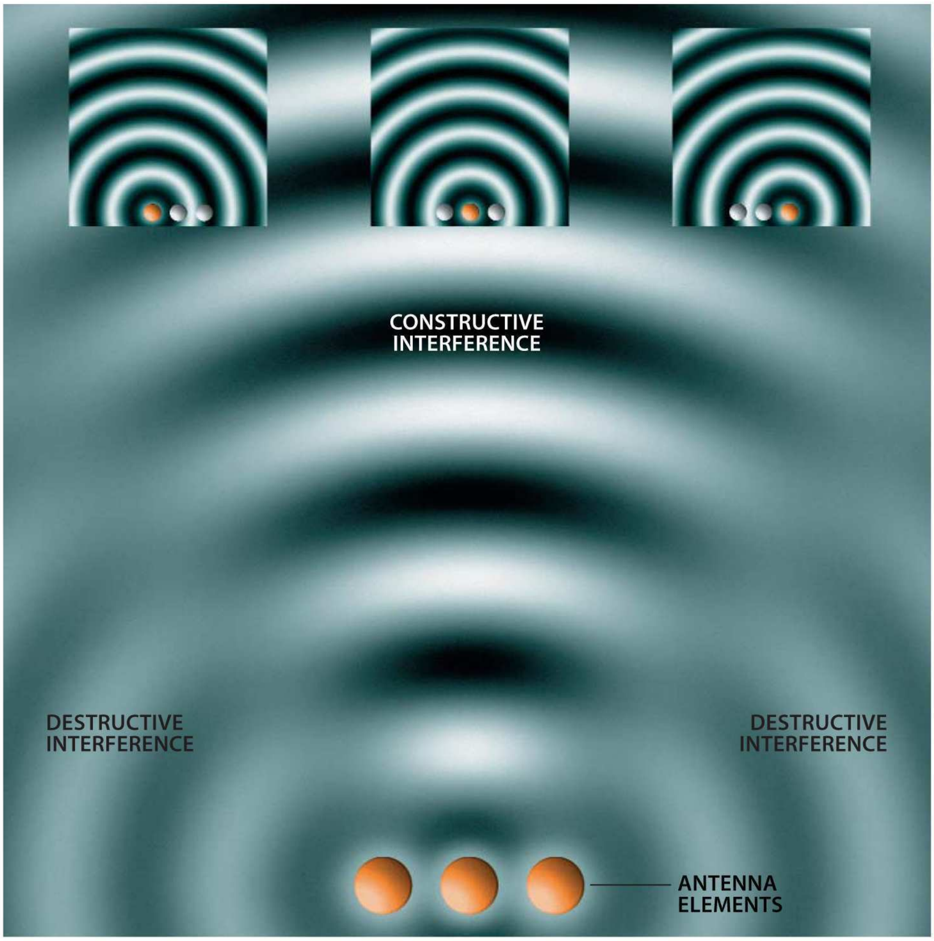
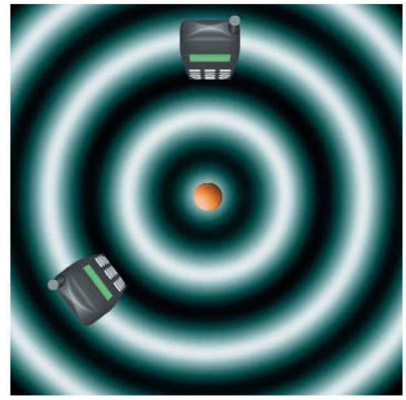
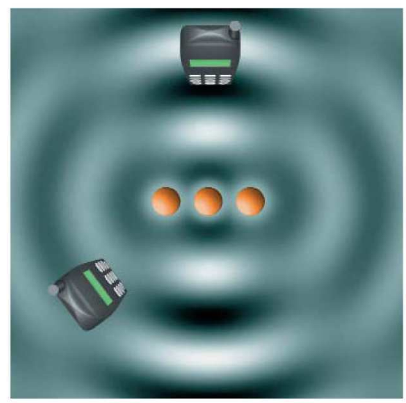


Each antenna element in an array transmits its own signal *(insets)*. Crests of a combined signal pile up, and their troughs overlap, forming narrow areas of constructive interference *(above)*. When a crest and a trough meet, they cancel each other out and form destructive interference.



A standard antenna transmits and receives a signal over a wide area. Users' signals within that region may interfere with one another.



A smart antenna directs constructive interference at the user to create a strong signal and reduce user interference.

By Tracy Staedter | Illustrations by John MacNeill

THE SMART ANTENNA

Using a mobile phone in an urban area is like trying to talk to a friend across a crowded room. There's a lot of interference, and background noise gets in the way of a clear signal. When you're at a party, you can solve the problem by moving within earshot. With mobile communications, your best bet is a smart antenna.

A smart antenna typically comprises an array of four to 12 antenna elements that transmit and receive signals from a base station. Unlike a traditional antenna that blankets a vast area with a signal, a smart antenna focuses radio energy in the vicinity of users. This reduces interference from other users who are accessing the same tower, and it extends the range of the signal. With less interference, service providers can increase capacity on their portion of the radio spectrum by as much as a factor of 20 (depending on the application), giving more users clearer signals.

Smart antennae are popping up all over Europe and Asia, thanks to companies such as ArrayComm of San Jose, CA. In the United States, however, there is only a smattering of these systems, many of which are the result of an agreement between Metawave Communications, in Redmond, WA, and Verizon Wireless. San Francisco–based Vivato announced plans to market an inexpensive smart antenna, which it claims will extend the range of the Wi-Fi data-transfer standard from a few dozen meters to several kilometers. For now, though, it seems that carriers are reluctant to invest the capital, so it may be a few more years before we're asking, "Can you download me now?" TR

For an animated version of this illustration, go to www.technologyreview.com/visualize/.

INFOGRAPHICS SOURCE: ARRAYCOMM

THE WEAKENING LINKS

The Western world was rightly concerned last year when China blocked its citizens' access to Google, the Internet's ubiquitous search engine. In addition to raising a hue and cry in the United States, a bevy of "hacktivists" scrambled to set up mirrored Google sites to thwart China's effort. Now China no longer blocks Google outright: it's just more selective in its censorship. If, in China, you type in "Falun Gong," the name of a dissident Chinese religious group, your Google search yields virtually no links. Most of us would agree this is a misguided effort by the Chinese government to suppress information, right?

But something similar is afoot in the United States. An accelerating trend to remove Internet links is being driven by two well-meaning but misguided pieces of legislation. The first, known as the Digital Millennium Copyright Act of 1998, says any Internet service provider can be sued and even shut down for linking to a site known to violate U.S. copyright laws. And the second, the recent legislation popularly known as the USA Patriot Act, makes it a crime to aid or abet terrorist organizations. Both laws are putting new pressures on the U.S. commitment to free speech.

Take the recent fracas at the University of California, San Diego. Last fall, the university's administration tried to force a student group to delete from its Web page a link to the Web site of the Revolutionary Armed Forces of Colombia, a violent Marxist insurgency. University officials claimed that the link violated the USA Patriot Act by providing "material support or resources" to a group that has been placed on the State Department's list of foreign terrorist organizations. Doesn't the drive to remove links—even to potentially unpleasant information—smack of the tactic we revile when practiced by the Chinese government?

The First Amendment is still sufficiently robust to have convinced university officials to back off from the hyperlink brouhaha—at least for the moment. I'm sure we will see other efforts to delete hyperlinks to "terrorist" information. In the meantime, I'm even more worried about the insidious censorship resulting from the Digital Millennium Copyright Act.

Consider, for instance, another Google-related censorship story. Last spring, Google removed links to Web pages critical of the Church of Scientology. Why? Because the creepy organization sent Google a letter of complaint, citing the Digital Millennium Copyright Act and claiming that Google was offering links to Web pages that infringed the Scientologists' copyrighted material. The Scientologists asserted that the search engine must either remove the links or face a court-ordered shutdown.

In letters to Google, the Church of Scientology alleges that its critics violate the law when they excerpt copyrighted and trademarked church documents and post them on Web sites. The critics say that the excerpts are essential to expose the dishonesty of the Church of Scientology. But the government's provisions in favor of copyright holders—in this case the Church of Scientology—have helped censor the critics by prompting search engines to sever links to the critics' sites. (For news about similar cases, visit chillingeffects.org, sponsored by the Electronic Frontier Foundation.)

After some hand wringing, Google found a way to continue to reference xenu.net, the anti-Scientology site: the company determined that a link solely to the group's home page is allowed under the law because the home page itself doesn't contain any instances of copyright infringement. (Google says the initial "delinking" of the home page was inadvertent.)

Some free-speech advocates cheered Google's refusal to knuckle under. But Google's government-mandated censorship continues. If you go to Google and type, "site:xenu.net leaflet," you'll see a note at the bottom of the page explaining that links to 10 Web pages have been removed. Is it just me, or does a state-sanctioned drive to suppress Google links about a religious group sound like the case of China and the Falun Gong?

Internet censorship isn't just for China anymore. A pair of misguided U.S. laws are prompting search engines to slash links for fear of incurring copyright and even criminal liability.

Perhaps the harshest of all the provisions of the copyright law are those that make it illegal to publish any information that might be used to circumvent anticopying technology embedded in software, CDs, DVDs, and any other medium. The situation has gotten so bad that when the software firm Red Hat published a patch to fix an error in its latest version of the Linux operating system, it declined to offer documentation to its U.S. users. Instead, it posted the technical literature on a European site—thefreeworld.net—that specifically prohibits U.S. citizens from accessing the documentation and warns that U.S. users could face jail time and heavy fines.

To combat some of the worst excesses of the law, U.S. Representative Rick Boucher (D-Virginia) is introducing legislation that adds badly needed fair-use provisions to the Digital Millennium Copyright Act. His proposed Digital Media Consumers' Rights Act would restore the legal right to publish copyrighted information—even about those evil "circumventing technologies"—as long as the information is explicitly for "scientific research into technological protection measures."

This legislation deserves support. With a heritage that includes such rabble-rousing pamphleteers as Thomas Paine and Samuel Adams, the United States has long championed freedom of speech. We ought not let our commitment falter on the journey into cyberspace. Otherwise, the most perilous link will be the glaring one between the United States and nations such as China that have no free-speech tradition at all. TR

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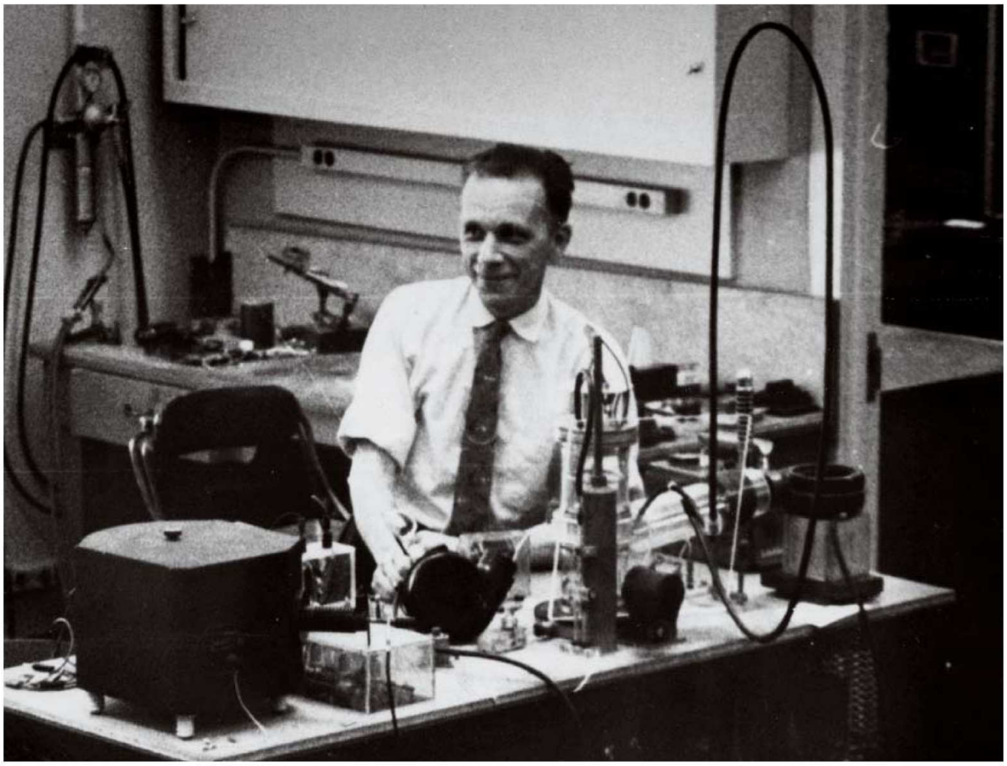

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NO P-N INTENDED
A cracked crystal launched the silicon revolution

When Russell Ohl began working at Bell Laboratories in 1927, vacuum tubes were seen as the future of electronics. It was his chance discovery, however, that led to the creation of both the transistor and the solar cell and helped spark the "silicon revolution."

In the late 1930s Ohl was a radio researcher trying to create a receiver that would be more effective than vacuum tubes. The tubes easily picked up low-frequency radio signals, but had trouble with higher frequencies such as those being tested in radar—a technology that was gaining importance as war brewed overseas. Ohl thought an alternative might lie in the crystal receiver, an antiquated radio device from the 1920s. He devoted himself completely to his research: when his workweek was shortened during the Depression, Ohl used his extra time to study crystal structure.

Crystal receivers were tricky, poorly understood devices. To get a signal, an operator would search the surface of a crystal with a metal strand for the "hot spot," which caused current flow in only one direction. After exhaustive experimentation, Ohl concluded that the best receivers were the elements now known as semiconductors. He theorized that purer materials would make better receivers and had special samples prepared for his tests.

Early in 1940 Ohl examined a silicon sample that had a crack down its middle. Something was strange about that crystal: when it was exposed to light, the current flowing between the two sides of the crack jumped significantly. Baffled, Ohl showed the bizarre sample to his Bell colleagues, who were equally amazed. No one had ever seen a photovoltaic reaction like it.

The researchers discovered that the crack was a dividing line between two impurities in the silicon. One type of silicon had an excess of electrons, the other a deficit. They named them p-type for positive and n-type for negative, and the barrier between the two was dubbed the p-n junction. Gradually, the group realized that photons give the excess electrons in the n-type material enough of an energy boost to cross the junction and produce a current.

Although Ohl's original crystals didn't produce nearly enough power for commercial use, his research into p- and n-type silicon led to Bell Labs' creation of the first modern solar cell in 1954. The first transistors also were based on the p-n junction. When Ohl held his unusual crystal to the light in 1940, he unwittingly began the transition from vacuum tubes to integrated circuits. —*Lisa Scanlon*

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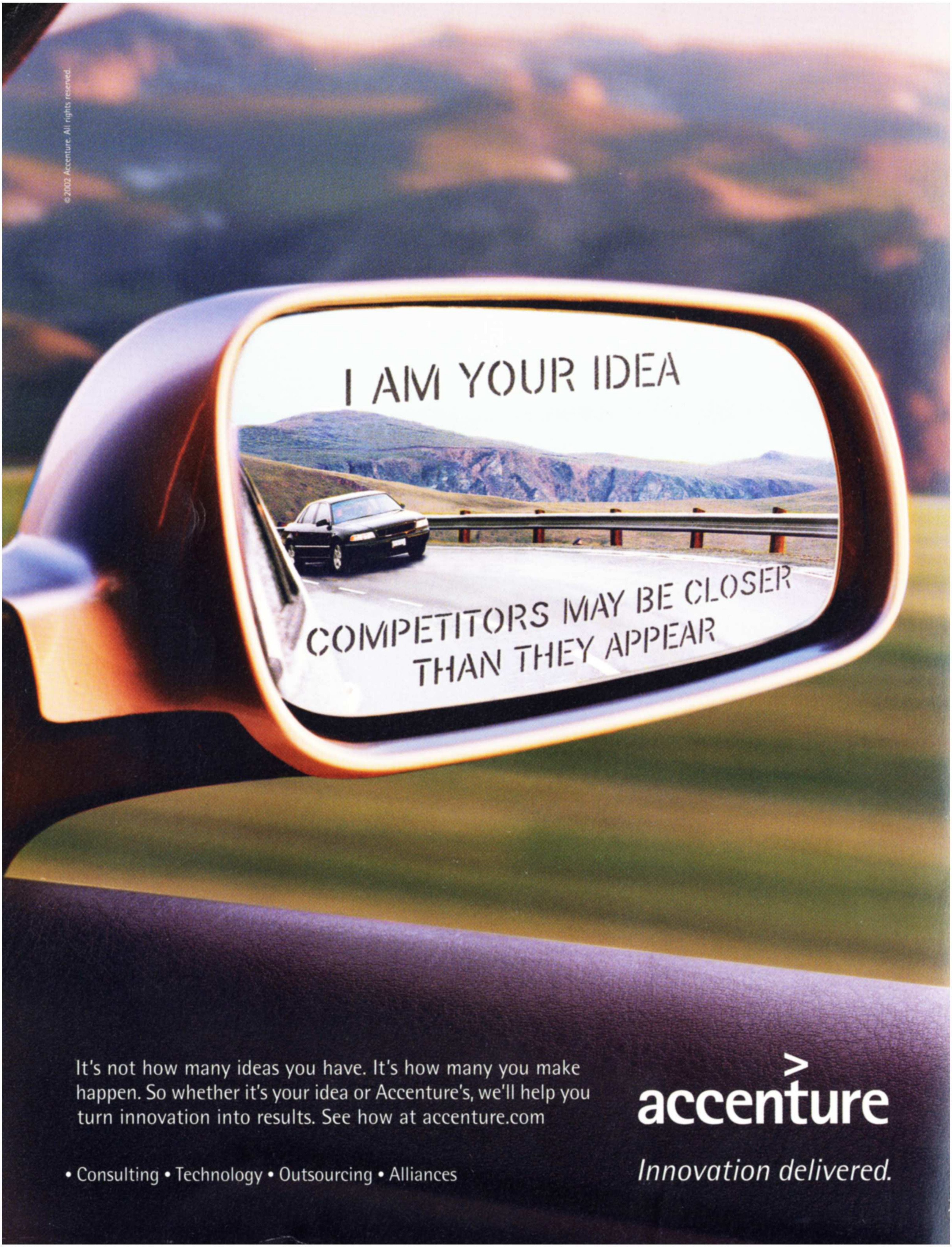
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